Supplementary Table 1. Identification of hecw-1 coding polymorphisms at amino acid positions 322 and 325 in 162 strains of C. elegans.

| Strain | hecw-1 | npr-1 | Strain | hecw-1 | npr-1 | Strain | hecw-1 | npr-1 | Strain | hecw-1 | npr-1 |
|--------|--------|-------|--------|--------|-------|--------|--------|-------|--------|--------|-------|
| AB1    | 322Y, 325Q | 215F | AB2    | 322C, 325Q | 215F | AB3    | 322C, 325Q | n.d. | AB4    | 322C, 325Q | n.d. | CB3191 | 322Y, 325Q | 215V |
| CB3192 | 322Y, 325Q | 215V | CB3193 | 322Y, 325Q | 215V | CB3194 | 322Y, 325Q | 215V | CB3195 | 322Y, 325Q | 215V | CB3198 | 322C, 325Q | 215F |
| CB4507 | 322Y, 325Q | 215V | CB4509 | 322Y, 325Q | 215V | CB4513 | 322C, 325Q | 215F | CB4518 | 322C, 325Q | 215F | CB4853 | 322C, 325Q | 215F |
| CB4853 | 322C, 325Q | 215F | CB4855 | 322C, 325Q | n.d. | CB4857 | 322Y, 325Q | 215F | CB4932 | 322Y, 325Q | 215F | CC1    | 322Y, 325Q | n.d. |
| CC2    | 322Y, 325Q | n.d. | CC3    | 322Y, 325Q | n.d. | DH424  | 322Y, 325Q | 215V | DR1344 | 322Y, 325Q | 215F | DR1346 | 322Y, 325Q | 215F |
| DR1346 | 322Y, 325Q | 215F | DR1348 | 322Y, 325Q | n.d. | DR1348 | 322Y, 325Q | 215F | DR1348 | 322Y, 325Q | 215F | DR1348 | 322Y, 325Q | 215F |
| DR1348 | 322Y, 325Q | 215F | DR1348 | 322Y, 325Q | n.d. | DR1348 | 322Y, 325Q | 215F | DR1349 | 322Y, 325Q | 215V | DR1350 | 322C, 325Q | n.d. |
| ED3005 | 322Y, 325Q | 215F | ED3005 | 322Y, 325Q | 215F | ED3011 | 322Y, 325Q | 215F | ED3011 | 322Y, 325Q | 215F | ED3017 | 322Y, 325Q | 215F |
| ED3017 | 322Y, 325Q | 215F | ED3017 | 322Y, 325Q | 215F | ED3021 | 322Y, 325Q | 215F | ED3024 | 322Y, 325Q | 215F | ED3040 | 322Y, 325Q | 215F |
| ED3040 | 322Y, 325Q | 215F | ED3040 | 322Y, 325Q | 215F | ED3042 | 322Y, 325Q | 215F | ED3042 | 322Y, 325Q | 215F | ED3042 | 322Y, 325Q | 215F |
| ED3042 | 322Y, 325Q | 215F | ED3042 | 322Y, 325Q | 215F | ED3042 | 322Y, 325Q | 215F | ED3064 | 322Y, 325Q | 215F | ED3052 | 322Y, 325Q | 215F |
| ED3052 | 322Y, 325Q | 215F | ED3052 | 322Y, 325Q | 215F | ED3072 | 322Y, 325Q | 215F | ED3072 | 322Y, 325Q | 215F | ED3077 | 322Y, 325Q | 215F |
| ED3077 | 322Y, 325Q | 215F | ED3077 | 322Y, 325Q | 215F | ED3077 | 322Y, 325Q | 215F | ED3077 | 322Y, 325Q | 215F | EG4788 | 322C, 325Q | n.d. |
| EG4788 | 322C, 325Q | n.d. | EG4788 | 322C, 325Q | n.d. | JU1088 | 322Y, 325Q | 215F | JU1088 | 322Y, 325Q | 215F | JU1171 | 322Y, 325Q | n.d. |
| JU1171 | 322Y, 325Q | n.d. | JU1171 | 322Y, 325Q | n.d. | JU1171 | 322Y, 325Q | n.d. | JU1171 | 322Y, 325Q | n.d. | JU1171 | 322Y, 325Q | n.d. |

n.d. not determined
Supplementary Figure 1. Genetic variation in *P. aeruginosa* lawn avoidance behaviour.

Time course of the *P. aeruginosa* lawn avoidance behaviour of N2, CB4856, RC301 and DA650 strains. Occupancy of the *P. aeruginosa* lawn was determined at indicated times. *P < 0.001* was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
Supplementary Figure 2. Positional mapping of the *P. aeruginosa* lawn avoidance phenotype difference between the CB4856 and DA650 strains.

| Phenotype     | No. of animals |
|---------------|----------------|
| DA650-like    | 85 (21.7%)     |
| CB4856-like   | 307 (78.3%)    |

The break point SNPs of E88 and I27 are haw42350 (at -7.67cM, **) and haw42334 (at -7.18cM, ***)
(a) The *P. aeruginosa* lawn avoidance phenotype of CB4856 is dominant relative to the lawn avoidance phenotype of DA650. A cross between CB4856 and DA650 animals yielded F1 progeny with *P. aeruginosa* leaving behaviour equivalent to that observed for CB4856. *P < 0.001* was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.

(b) We observed that approximately ¼ (85 out of 392; 21.7%) of the randomly selected single F2 progeny from a cross between CB4856 and DA650 animals gave rise to corresponding F3 populations that exhibited *P. aeruginosa* lawn avoidance phenotypes corresponding those observed for DA650. These data suggest a substantial contribution from a single locus in determining the difference in *P. aeruginosa* lawn avoidance behaviour between CB4856 and DA650.

(c) Because the DA650 strain was derived from outcrossing the *npr-1 215F* allele of RC301, *npr-1(g320)*, with N2, we proceeded to use single nucleotide polymorphisms (SNPs) between N2 and CB4856 to identify the genetic locus responsible for the difference in lawn leaving phenotypes between DA650 and CB4856. Shown is a schematic of the 25 kilobase (kb) interval responsible for the delayed *P. aeruginosa* lawn avoidance behaviour in CB4856. Positional SNP mapping derived from the analysis of 1000 F2 recombinants from a cross between CB4856 and DA650 defined a 25 kilobase (kb) interval on Chromosome III between SNPs haw42334 (-7.18 cM) and haw42350 (-7.07 cM). E88 and I27 are the recombinant strains with the most informative break points. Right: *P. aeruginosa* lawn avoidance phenotypes of the E88 and I27 at t = 32 h. *P < 0.001* was determined by the ANOVA multiple comparisons test. n.s. indicates not significant. Error bars indicate s.e.m.

(d) We carried out rescue experiments involving transformation of the DA650 strain with genomic DNA fragments from CB4856 to identify the sequence sufficient to confer DA650 with a CB4856 *P. aeruginosa* lawn avoidance phenotype. We found that an 8 kb fragment of CB4856 genomic sequence within this 25 kb interval, encompassing only the F45H7.6 gene (Fig. 1c), was sufficient to confer DA650 with the delayed CB4856 lawn-leaving phenotype. Shown in (d) are the *P. aeruginosa* lawn avoidance data for DA650 carrying an 8kb genomic fragment containing *hecw-1* from CB4856. *P < 0.001* was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
Supplementary Figure 3. Loss-of-function of *hecw-1* confers enhanced pathogen avoidance behaviour.

(a) *hecw-1(ok1347)* confers an early avoidance behaviour after 5 h exposure to *P. aeruginosa* PA14. An 8 kb *hecw-1* genomic fragment (depicted in Fig. 1c) rescues the phenotype. The *hecw-1(ok1347)* mutant contains a deletion of 2208 nucleotides (Fig. 1c), which is predicted to remove the second WW domain and part of the HECT domain of the HECW-1 protein, and thus represents a putative null. (b) RNAi by bacterial feeding of *hecw-1* in N2 and DA650 backgrounds contributes to earlier *P. aeruginosa* PA14 leaving times compared to RNAi treatment with vector only (L4440) control. * P < 0.01 was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
**Supplementary Figure 4. Structure modeling of the region containing hecw-1 polymorphism.**

(a) Sequence alignment of the region of HECW-1 containing Y322 and Q325 in orthologues of *C. elegans* HECW-1. Residues 322 and 325 of *C. elegans* HECW-1 reside in a conserved linker region that lies between the two WW domains (Fig. 1d).

(b) Structural model of the *C. elegans* HECW-1 region containing the Y322 and Q325 residues (shown to extend from the surface of the structure). Based on the crystal structure of a 109 amino acid fragment of the homologous human HECW1 protein that encompasses this linker domain and the second WW domain and has been deposited into the Protein Data Bank (structure 3L4H), we developed a structural model of the corresponding domains of the *C. elegans* HECW-1 protein. In the HECW-1 structural model, Q325 lies at the end of a helix in the region of a tight helical turn, with the side chain extending from the surface of the protein, and the side chain of Y322 also extends from the same surface region of the protein. Whereas the E3 ligase activity is predicted to be in the HECT domain, the tandem WW domains and adjacent sequences are implicated in substrate recognition function\(^4\). Our model suggests that the 325P and 322C polymorphisms may alter a protein-protein interaction interface on the surface of HECW-1 without a radical disruption of protein structure. We generated the model with MODELLER\(^5\). The model in Supplementary Fig. 4b is rendered using PyMOL.
Supplementary Figure 5. OLL neuron pair expression and functional characterization of a HECW-1::GFP translational fusion protein under the control of hecw-1 promoter.

(a) Fluorescence of the hecw-1p::HECW-1::GFP fusion protein in the region of the anterior ganglion. Nerve ring signals were contributed by transformation marker mec-4p::gfp. Scale bar indicates 10 µm. (b) P. aeruginosa lawn avoidance behaviour of the hecw-1(ok1347) mutant carrying a hecw-1p::hecw-1 cDNA::gfp transgene. The hecw-1p promoter is comprised of the 0.9 kb sequence upstream of the start of the hecw-1 coding sequence. * P < 0.01 was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
Supplementary Figure 6. Expression of HECW-1::GFP fusion protein in PVD does not rescue the hecw-1(ok1347) phenotype.

(a) Fluorescence of the hecw-1p::HECW-1::GFP fusion protein in the region of the anterior ganglion. Nerve ring signals were contributed by transformation marker mec-4p::gfp. Scale bar indicates 10 µm. (b) P. aeruginosa lawn avoidance behaviour of the hecw-1(ok1347) mutant carrying a hecw-1p::hecw-1 cDNA:gfp transgene. The hecw-1p promoter is comprised of the 0.9 kb sequence upstream of the start of the hecw-1 coding sequence. * P < 0.01 was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
Supplementary Figure 7. A role for the OLL neuron pair and hecw-1 in mechanosensation.

(a) Nose Touch defects were observed from animals in which OLL was genetically ablated by expression of csp-1b under the control of ser-2d promoter and hecw-1(ok1347) animals. The Nose Touch phenotype of hecw-1(ok1347) was rescued by hecw-1::gfp expression under the control of either hecw-1p or ser-2dp (OLL expression). The glr-1(n2461) mutant was used as a positive control of Nose Touch phenotype. (b) The hecw-1(ok1347) mutation had no effect on the Nose Touch phenotype in the npr-1(ky13) mutant background. (c) Laser ablation of OLL causes a Nose Touch phenotype. ASH ablation was carried out in parallel as a positive control for the Nose Touch phenotype. Laser ablation was performed using the ZD654 qdEx23 [ser-2p::GFP; myo-2p::mCherry] and PY1058 [oyIs14 V; lin-15AB(n765ts) X] strains to identify the OLL and ASH neurons respectively. These Nose Touch phenotype assays were performed blind with random labels provided by a second experimenter. * P < 0.01 was determined by the ANOVA multiple comparisons test. For each experiment, 20 or more animals were tested and each animal was tested ten times. Error bars indicate s.e.m.
Supplementary Figure 8. NPR-1 expression in the RMG interneuron is required for the hecw-1(ok1347) P. aeruginosa lawn avoidance phenotype. 

(a) A transgenic npr-1 genomic construct partially rescued the hecw-1(ok1347) P. aeruginosa PA14 lawn avoidance phenotype in the npr-1(ky13):hecw-1(ok1347) double mutant. (b) The expression of npr-1 cDNA in RMG and ASE under the control of flp-5 promoter partially rescued the hecw-1(ok1347) P. aeruginosa PA14 lawn avoidance phenotype in the hecw-1(ok1347) and npr-1(ky13) double mutant background. These data suggest that NPR-1 activity in RMG is sufficient for the modulation of pathogen avoidance behavior by HECW-1, although the observed partial rescue does not rule out the possibility that NPR-1 expression in neurons other than RMG may also contribute to the hecw-1 mutant phenotype. * P < 0.01 was determined by the ANOVA multiple comparisons test. Error bars indicate s.e.m.
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