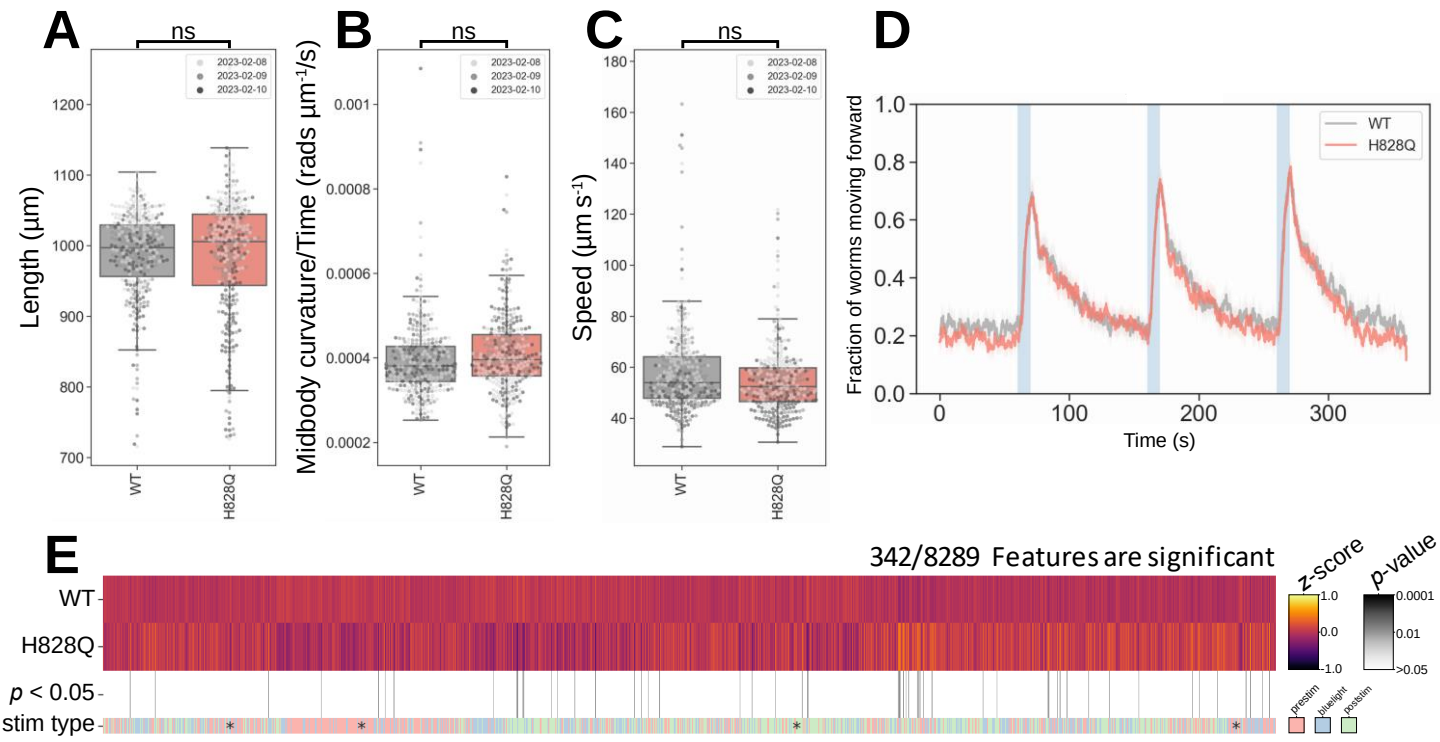


**Figure S1. H828Q substitution causes no behavioural phenotype in the absence of treatment with $CuCl_2$.**

**A-C.** These plots show no difference between untreated H828Q and WT worms for the key behavioural features identified as being significant in the presence of excess Cu (see Figure 5). Individual points on the boxplots represent averaged values of 3 worms per well in the tracking plates, and statistical significance between strains was calculated using block permutation t-tests ($n$ = 10,000 permutations) corrected for multiple comparisons using the Benjamini Hochberg correction. **D.** There is no difference in locomotion, or the response of untreated mutant and WT worms to stimulation with blue light (blue shaded regions). Coloured lines represent averages of the detected fraction of worms moving forwards across all biological replicates and shaded areas represent the 95% confidence intervals. **E.** Behavioural fingerprint of the entire set of 8,289 behavioral features extracted by Tierpsy for WT and H828Q worms, with the total number of statistically significant features shown above the heatmap. As the small number significant features only relate to highly-variable Tierpsy outputs, primarily standard deviation and interquartile range values, we consider there to be no robust phenotypic difference between untreated H828Q and WT behaviour. The stim type barcode denotes when during image acquisition the feature was extracted: pre-stimulation (pink), blue light stimulation (blue), and post-stimulation (green). Asterisks indicate the position of the selected features presented in plots A-D within the entire feature set and the colour maps (right) represents the normalised $z$-score or calculated $p$-value for each feature. All behavioural experiments were conducted across 3 independent days and all data shown represents well averaged values (3 worms per well), with $n \geq 116$ wells for each strain.

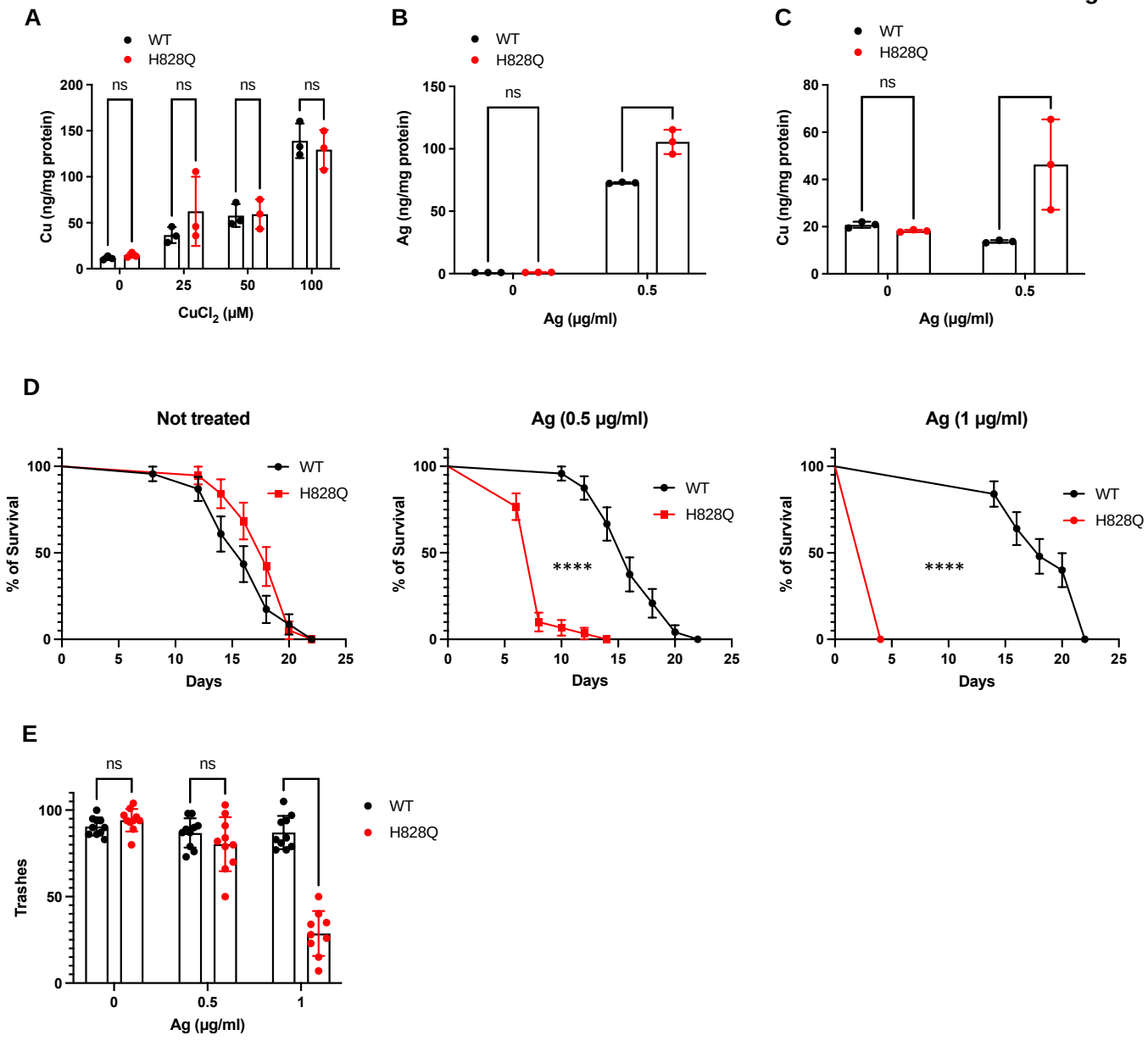


**Figure S2. Metal content and impact of silver in WT and *cua-1(knu790*[H828Q]) *C. elegans* strains.**

**A-C.** Wild type (WT) and mutant (H828Q) animals were grown for 3 days in the presence of copper (A) or silver (B, C) at the indicated concentrations. Then the animals were collected and subjected to AAS for Cu and Ag detection. Mutants do not manifest differences in Cu content compared to WT controls upon Cu treatment (A), while exposure to silver causes higher accumulation of both Ag and Cu in mutant animals (** $p<0.01$, **** $p<0.0001$; two way ANOVA; n=3 experiments). **D.** The graphs show survival curves of WT and mutant animals grown in the presence of different Ag concentrations. Incubation with Ag significantly shortened the lifespan of mutant animals (**** $p<0.0001$; Mantel-Cox test; n≥20 animals). **E.** Quantification of thrashing moves revealed that 1μg/ml Ag suppresses motility of mutant animals (**** $p<0.0001$; two way ANOVA; n=10 animals).

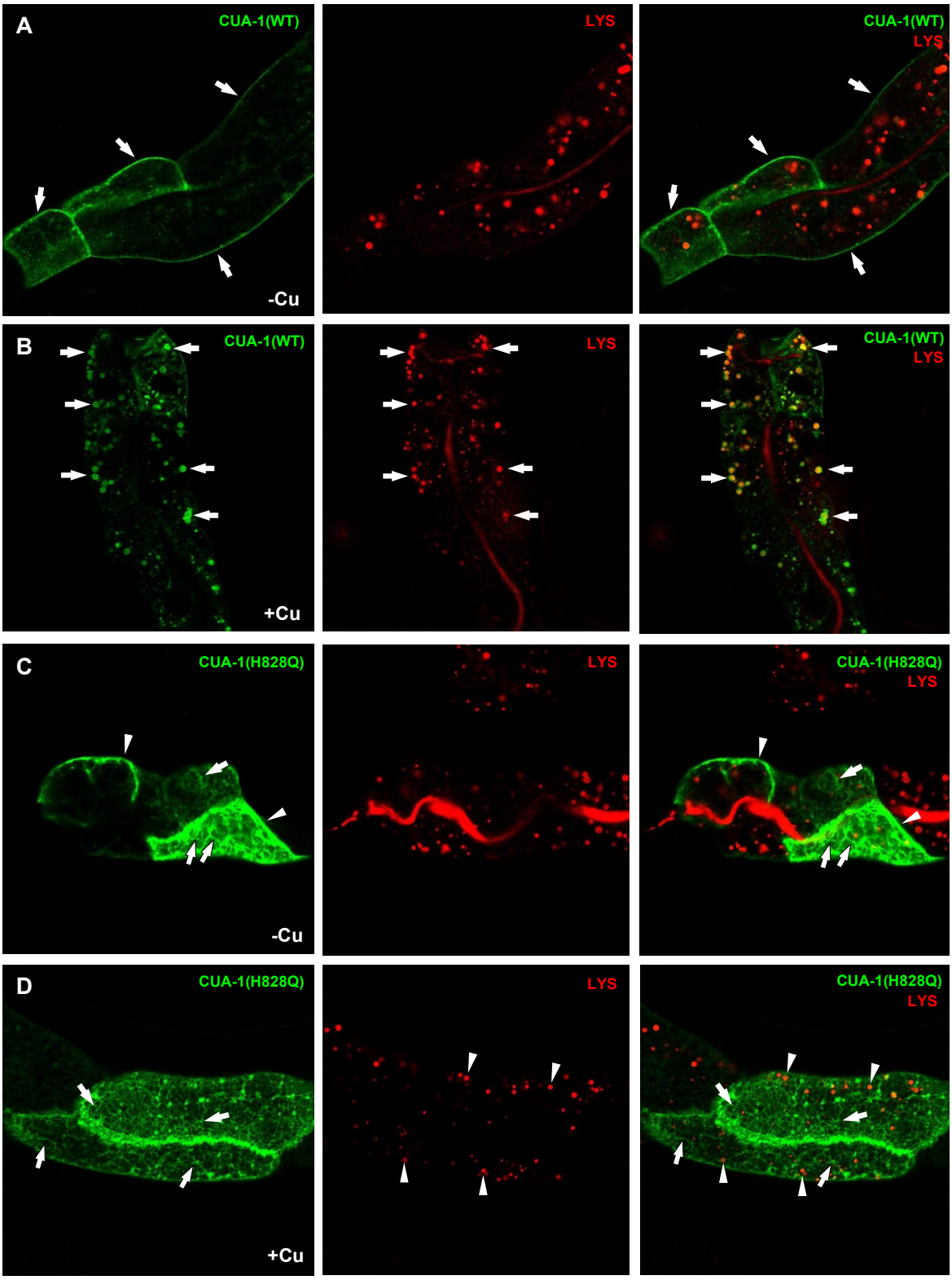


**Figure S3. Localization of WT and H828Q variants of CUA-1.**
GFP-tagged versions of WT (A) or H828Q (B) variants of CUA-1 were expressed in intestinal cells of C.elegans grown at normal conditions (A, C) or treated overnight with 100 µM $CuCl_2$ (B, D). The animals were loaded with lysotracker (LYS) to label lysosomes and investigated using confocal microscopy. **(A)** Arrows indicate CUA-1(WT) at the plasma membrane. **(B)** Cu treatment causes redistribution of CUA-1(WT) to LYS-positive lysosomal structures (Arrows). **(C)** Arrows show localization of CUA-1(H828Q) in the ER membrane network, while cell-surface located mutant protein is indicated by arrowhead. **(D)** Significant amount of CUA-1(H828Q) remains in the ER in Cu-treated animals (Arrows), while most of lysosomes do not receive the mutant protein (Arrowheads). Scale bar: 20 µM (A-D).