

Figure S1. iHg accelerates proteotoxic stress. Representative fluorescent micrographs of 1, 2, 3, and 4 day old, adult hermaphrodites of a *C. elegans* proteotoxic stress model that expresses homopolymeric repeats of 35 glutamines fused to yellow fluorescent protein (Q35::YFP) in body wall muscle cells (Morley et al., 2002). Hermaphrodites were mock-treated or exposed to 50 μ M iHg for 24, 48, and 72 hours. Bar, 100 μ M. Mock-treated showed an age-related change from a mostly smooth distribution of yellow fluorescence along the body wall muscles to a dotted pattern of aggregated polyQ. Hermaphrodites exposed to iHg exhibit an acceleration of the age-related change to aggregated polyQ with a first appearance at adult day 2. Note that the two depicted

untreated hermaphrodites for the 48-hour time-point reflect the wide range of aggregation progression observed in this cohort.

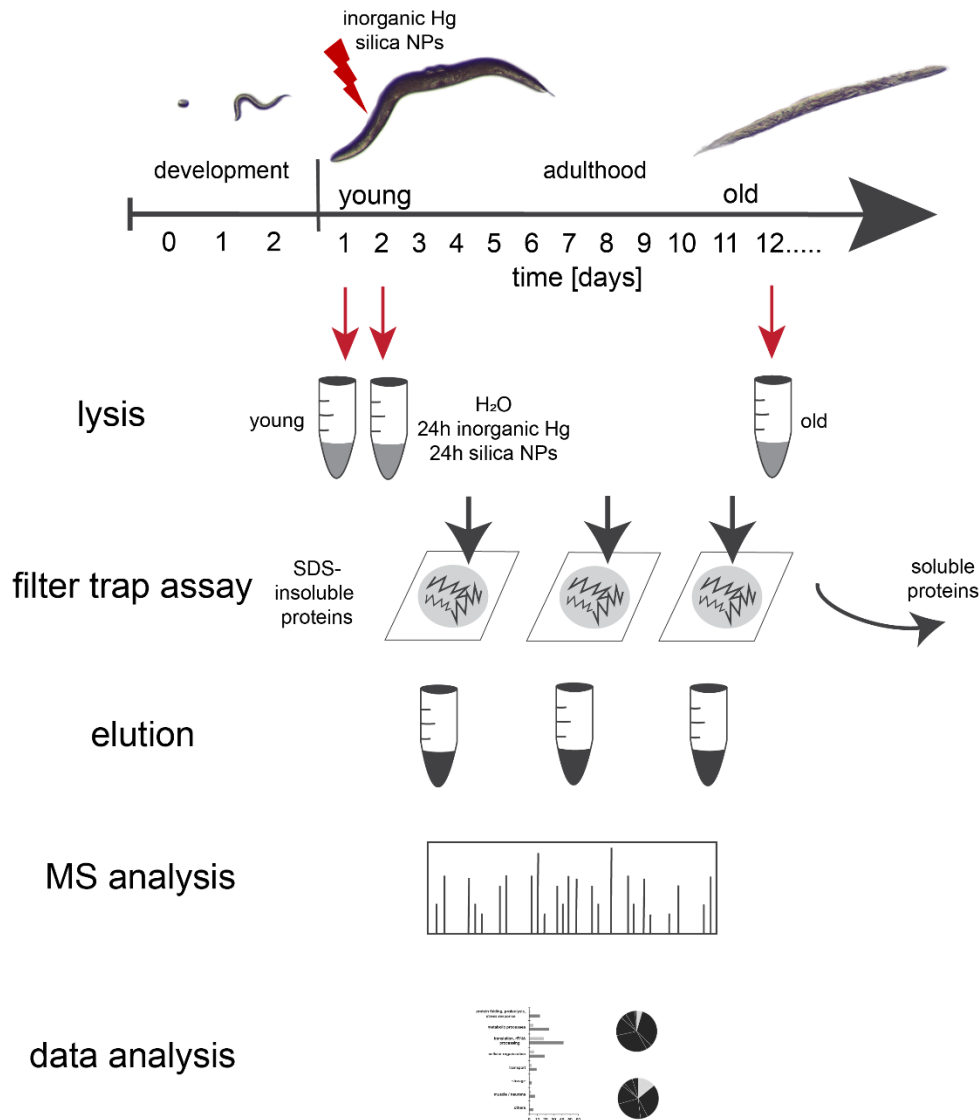


Figure S2. Schematic of the experimental design of the different aggregate characterizations. For the iHg- and silica NPs- induced aggregate analysis, synchronized wild type *C. elegans* (N2) were mock-treated, or exposed to iHg or silica NPs on adult day 1 for 24 hours before lysis. For the age-induced aggregate analysis, synchronized wild type *C. elegans* (N2) were lysed on adult day 1 as “young” or on adult day 12 as “old”. SDS-insoluble proteins were trapped on filter, eluted with 6M guanidinium hydrochloride, followed by mass spectrometry (ESI-LC/MS), and data analysis including data mining. Note that the experiments to identify the iHg, the silica NPs, and the age-induced aggregate networks were done separately.

GO-group: protein folding, proteolysis, stress response

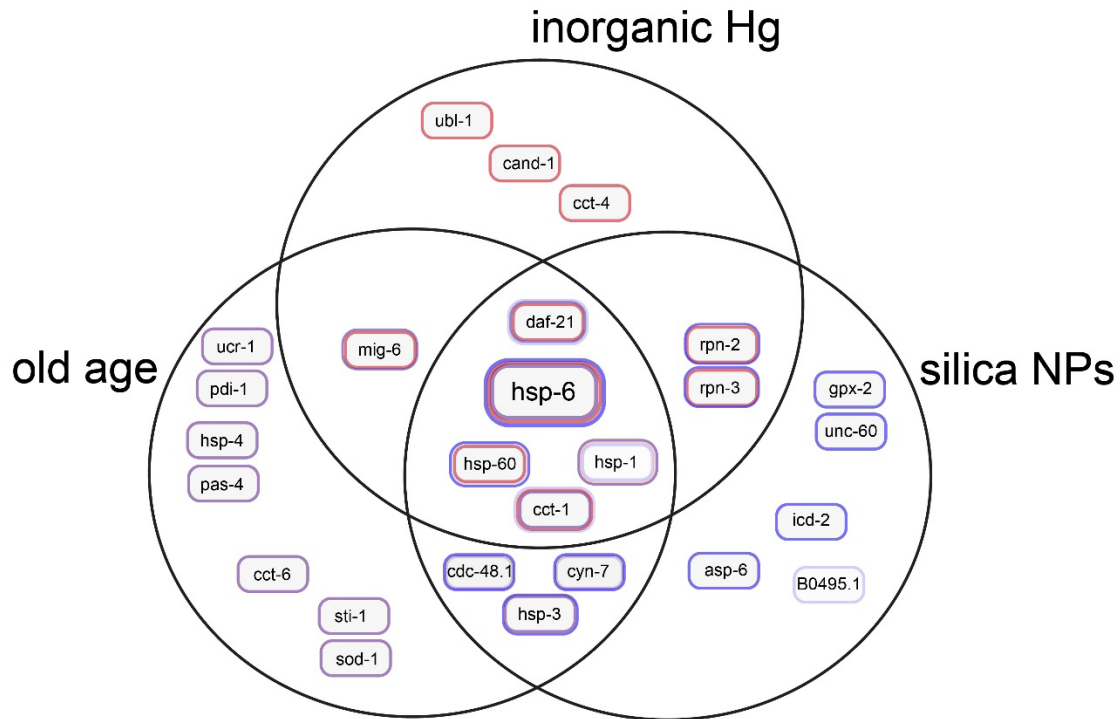


Figure S3. GO-group: protein folding, proteolysis, and stress response. Venn diagram of identified insoluble proteins categorized according their biological process protein folding, proteolysis, and stress response classified by the PANTHER databank (Mi et al., 2013) in the iHg- (red), silica NPs- (blue, (Scharf et al., 2016)), and age-induced (purple) aggregate network. The boxes indicate the number of proteins identified in the ground and specific aggregate, respectively.

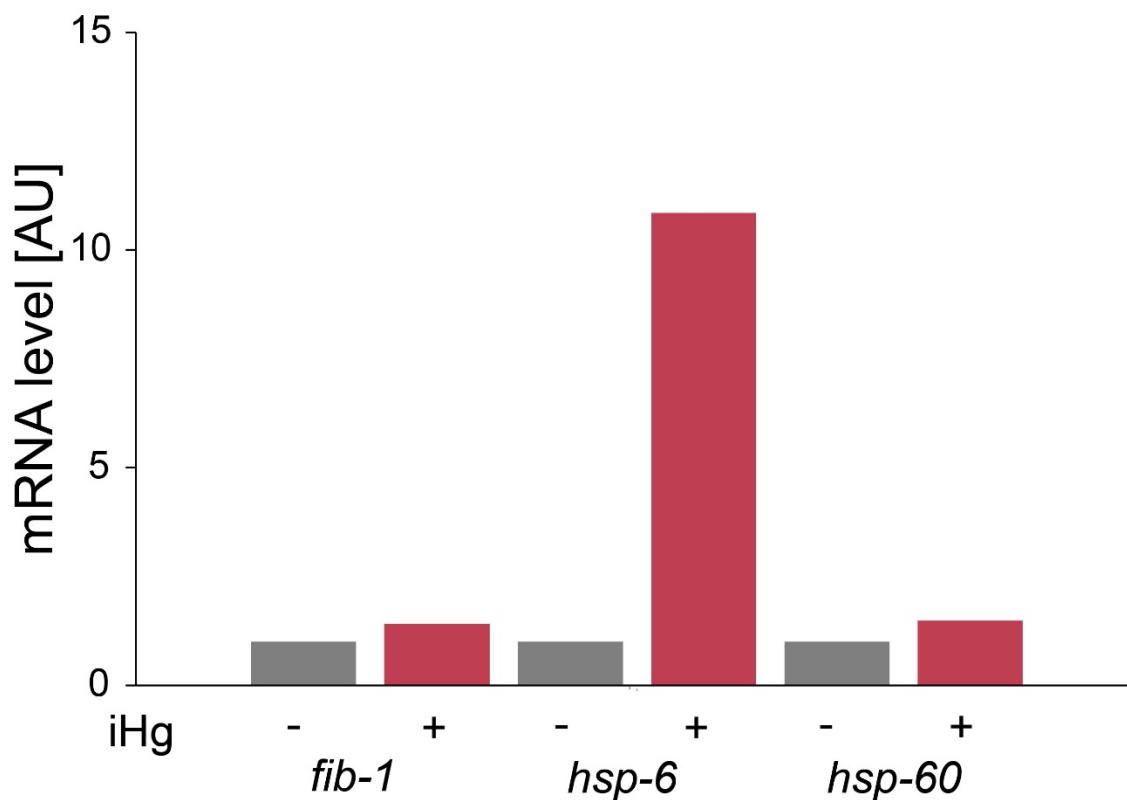


Figure S5. Expression is not correlated with protein aggregation. The bar graph shows mRNA levels of *fib-1*, *hsp-6*, and *hsp-60* in H₂O-treated versus 50 μ M iHg-treated wild type *C. elegans*. RNA levels were determined by qPCR in two independent experiments and show fold change compared to H₂O control.