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Bursting worms: an osmoregulatory role for FMO-4 in *Caenorhabditis elegans*

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Flavin-containing monooxygenases (FMOs) catalyse the oxidation of structurally diverse substrates including drugs, pesticides and other environmental pollutants and chemicals. To investigate the physiological role of FMOs, we used the reverse genetics approach to analyse an FMO homologue in the model organism *Caenorhabditis elegans*. FMO-4 is a hypodermally-expressed *C. elegans* protein that possesses a consensus NADP-/FAD-binding motifs and a D(X)3(L/F)ATGY(X)4P motif found in all mammalian FMOs that have the ability to catalyse *N*-oxidation. We demonstrate that recombinant *C. elegans* FMO-4 heterologously expressed in insect cells via the baculovirus system was able to *N*-oxidize the archetypal mammalian FMO substrate benzydamine (BZ). We further show that *fmo*-4 mutants were acutely sensitive to the presence of BZ suggesting a biological function in drug detoxification. Importantly, these studies confirm the osmoregulatory role of FMO-4 with *fmo-4* mutants showing high sensitivity to hypo-osmotic stress exhibiting the formation of stiff rod-like body upon exposure to water indicative of high internal hydrostatic pressure and the subsequent worm body rupture that resulted in bursting out of internal coelomic contents.