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## MEETING ABSTRACTS

# THE *Caenorhabditis elegans* PHARYNX AS A MODEL SYSTEM TO INVESTIGATE AND MITIGATE AGAINST THE EFFECTS OF ANTI-CHOLINESTERASE DRUGS

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*C. elegans* is a free-living worm widely used as model to study neurotoxicology. Despite its simplicity, *C. elegans* has a high level of genetic and molecular conservation with vertebrates. Similar to mammals, intoxication with anti-cholinestereses triggers the accumulation of synaptic acetylcholine causing continuous stimulation of both nicotinic and muscarinic receptors, hypercontracting the muscles of the worm[1]. The pharynx, the nematode feeding organ, depends on cholinergic function. Pharyngeal movements, readily observed in whole organism, are disrupted by impairments in cholinergic transmission. Therefore, quantitative analysis of pharyngeal structure and function has excellent potential to probe anti-cholinesterase mode of action that may translate to human toxicology.

We establish the $IC_{50}$ values for the carbamate aldicarb and the organophosphates paraoxon-ethyl, paraoxon-methyl and DFP, highlighting a distinct dose-time dependence inhibition of pharyngeal activity. In recovery experiments, aldicarb and paraoxon-ethyl but not paraoxon-methyl or DFP intoxicated worms recover the pharyngeal function onto empty and oxime plates. A cycle of aldicarb intoxication-recovery-intoxication revealed aldicarb-induced plasticity as a reduced sensitivity of pre-conditioned worms to a subsequent drug exposure. We investigated molecular determinants of this plasticity by using uncoordinated locomotion and reduced pharyngeal movement mutant worms due to impairments in cholinergic transmission. Interestingly, preconditioned mutant worms exhibits a switch in the aldicarb-induced plasticity observed in wild type, becoming more sensitive to post-exposure of aldicarb. Defining the molecular identity of this mutant will reveal pathways that mediate cholinesterase induced structural reorganization at the pharyngeal NMJ. Thus, the drug and genetic tractability of *C. elegans* offers a new route to anti-cholinesterase poisoning antidotes.

*Keywords: anti-cholinesterase intoxication; cholinergic plasticity; C. elegans*

### References

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