366 Zebrafish Models For Human Acute Organophosphorus Poisoning

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Organophosphorus compounds (OP) are currently the most commonly used pesticides in the world and its use might result in acute poisoning, with around 3 million cases and 300,000 deaths annually. The molecular initiating event leading to organophosphorus compounds poisoning is the inhibition of acetylcholinesterase (AChE), resulting in the accumulation of the neurotransmitter acetylcholine (ACh) in the cholinergic synapses. However, the pathways conducting to some of the adverse outcomes are not well-understood. Zebrafish is being increasingly used as a model species for both ecological and human health risk assessment. Although the modes of action (MoA) leading to toxicity for these types of pesticides have already been analyzed in zebrafish, these analyses have been performed during embryonic development and therefore, are more related with the developmental toxicity than with the OP poisoning.

In this study we use a prototypic OP compound, chlorpyrifos-oxon (CPO), to develop a zebrafish model of OP poisoning using a set of molecular markers. The acute effects of mild, moderate, and high CPO concentrations on zebrafish larvae have been studied at different levels of organization including molecular (transcriptomic analysis by RNAseq, biochemical responses), cellular, tissue and organismal (gross morphology, behavioral effects [visual motor response (VMR) and touch-evoked escape response]). Three phenotypes were identified by gross-morphology and behavioral analysis. In conclusion, the adverse outcome pathways of the different phenotypes have been dissected empirically and the results obtained show that exposed zebrafish mimic many aspects of the human OPP, therefore confirming the use of zebrafish larvae as a suitable model to identify new antidotes against cholinergic syndrome.