ECTONUCLEOTIDASES AND ZEBRAFISH: TOXICOLOGICAL AND PHARMACOLOGICAL IMPLICATIONS

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It has been shown the involvement of ectonucleotidases in several physiological and pathological conditions able to promote synaptic plasticity, such as memory, epilepsy, and ischemia. To further our understanding of basic mechanisms underlying neurodegeneration and synaptic plasticity novel treatments requires additional animal model research. One strategy would be the development and characterization of new animal models, specifically those that are amenable to rapid drug screening and genetic manipulation. Zebrafish (*Danio rerio),* are small freshwater teleosts rapidly emerging as an important model organism in genetics and developmental neurobiology. Several neurotransmitter systems have been already described in zebrafish. Among them, the purinergic system, in which ATP acts as an important neurotransmitter and neuromodulator. Our laboratory has characterized the presence of NTPDases (nucleoside triphosphate diphosphohydrolases) and 5´-nucleotidase activities in zebrafish brain membranes. Considering the important role played by the purinergic system, we evaluated this neurotransmitter system as a potential target of neurotoxic compounds. Thus, we analyzed the effect of heavy metals and organic compounds on nucleotidase activities. The effect of lead, mercury, and copper was investigated on nucleotidases from zebrafish CNS. Lead, mercury, and copper promoted changes in ATP, ADP, and AMP hydrolysis after 24h, 96h, and 30 days of treatment. The treatment with copper sulphate during 24 and 96h also altered NTPDases and 5'-nucleotidase mRNA transcript levels. The acute treatment with 0.5 and 1% methanol or ethanol promoted a significant decrease in ATP and ADP hydrolysis, but there were no changes in ecto-5´-nucleotidase activity. The use of zebrafish for drug screening is an important pharmacological tool and we have shown that antipsychotics are able to inhibit nucleotide hydrolysis in zebrafish. Therefore, these enzymes may be important to the evaluation of neurotoxic targets for contaminants and as pharmacological tools for drug screening using an emergent and promising animal model, such as zebrafish.

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