ABSTRACT JSOT2021

Title:

ZEBRAFISH, A NOVEL KEY PLAYER FOR HUMAN RISK ASSESSMENT: latest advances on developmental neurotoxicity from an international consortium.

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TEXT

Exposure to chemicals during the first phases of development may play an important role in the manifestation of neurodevelopmental disorders and could result in cognitive disabilities. Currently, the prevalence of neurodevelopmental disorders exceeds 15% worldwide.

Developmental neurotoxicity (DNT) entails one of the most complex areas in toxicology, since development of the central nervous system is an intricate process involving multiple events, each of them representing a different window of vulnerability to chemical exposure.

Critical DNT data and mechanistic information for thousands of chemicals are still missing, mainly due to the limitations of currently approved DNT *in vivo* testing. For that reason, a pressing priority for the Organization for Economic Co-Operation and Development (OECD) is to generate a guideline using new alternative methods (NAMs) for a faster and more effective DNT assessment. The aim of this study is to demonstrate the added value of the zebrafish model inside the proposed *in vitro* battery for human risk assessment.

The nervous system, the different neuronal types and neurotransmitters are well studied and conserved between zebrafish and humans, in addition to high genome similarity. The advantage of the zebrafish model is that the entire brain development occurs within a relatively short period, and effects of chemicals on brain development and behaviour can be tested in a whole organism and its complex systems.

Here we present the results of an inter-laboratory studies aimed at the establishment of a harmonized protocol for DNT assessment using zebrafish-based assays. The zebrafish larval

system has been challenged with 28 known toxic chemicals followed by standard behavioural experiments. The results obtained pave the way for the integration of the zebrafish model in the novel OECD guidance document as a reliable alternative model for the improvement of human DNT prediction. (This abstract does not necessarily reflect EPA policy).