

Zebrafish holds clue to drug-resistant epilepsy: NIH

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Singapore: According to a research by scientists at the University of California, San Francisco (UCSF), US, zebrafish carrying a specific mutation may help researchers discover treatments for Dravet syndrome (DS), a severe form of pediatric epilepsy that results in drug-resistant seizures and developmental delays.

Dr Scott C Baraban and his colleagues at UCSF carefully assessed whether the mutated zebrafish could serve as a model for DS, and then developed a new screening method to quickly identify potential treatments for DS using these fish.

This study was supported by the National Institute of Neurological Disorders and Stroke (NINDS), which is part of the National Institutes of Health (NIH), and builds on pioneering epilepsy zebrafish models first described by the Dr Baraban's laboratory in 2005. Dravet syndrome is commonly caused by a mutation in the *Scn1a* gene, which encodes for Nav1.1, a specific sodium ion channel found in the brain. Sodium ion channels are critical for communication between brain cells and proper brain functioning.

The researchers found that the zebrafish that were engineered to have the *Scn1a* mutation that causes DS in humans exhibited some of the same characteristics, such as spontaneous seizures, commonly seen in children with DS. Unprovoked seizure activity in the mutant fish resulted in hyperactivity and whole-body convulsions associated with very fast swimming. These types of behaviors are not seen in normal healthy zebrafish.

“We were also surprised at how similar the mutant zebrafish drug profile was to that of Dravet patients,” said Dr Baraban. “Antiepileptic drugs shown to have some benefits in patients (such as benzodiazepines or stiripentol) also exhibited some antiepileptic activity in these mutants. Conversely, many of the antiepileptic drugs that do not reduce seizures in these patients showed no effect in the mutant zebrafish.”

In this study, the researchers developed a fast and automated drug screen to quickly test the effectiveness of various compounds in mutant zebrafish. The researchers tracked behavior and measured brain activity in the mutant zebrafish to determine if the compounds had an impact on seizures.