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Exploring the anti-seizure potential of selective PI3K inhibitor in zebrafish model of pentylenetetrazole induced seizure

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The role of mammalian target of rapamycin (mTOR), an evolutionary serine/threonine protein kinase, has been well documented in several disorders. In epilepsy research, mTOR pose as a very exhilarating target, as inhibition of its hyperactivation has been found to be effective in suppression of epilepsy and epileptogenesis. However the precise mechanism for the aberrant expression of mTOR, leading to the overexpression of its downstream genes, still remains blurred. Preclinical and clinical studies have revealed that decrease in PI3K/AKT/mTOR pathway hyperactivation have considerably reduced seizures. Hence, our study was designed to explore the anti-seizure potential of selective PI3K inhibitor (morpholine containing compound) on zebrafish model of pentylenetetrazole induced seizure. Zebrafish larvae of 7 days post fertilization were subjected to different concentrations of the selective PI3K inhibitor, following which they were exposed to pentylenetetrazole and recordings were scored on a 3 point scale. The best therapeutic concentration was selected and it was tested on adult zebrafish. Furthermore, fish brains were isolated and expressions of genes were studied in comparison to the epileptic fish. The results showed that the inhibitor distinctly reduced the seizure state in both larvae and adult fish in combination to decreasing the expression of various genes of the PI3K/AKT/mTOR pathway. These findings concluded that selective PI3K inhibitor has anti-seizure potential and can be explored in the near future as a potential antiepileptic.

Biography

Arindam Ghosh Mazumder is a Senior Research Fellow, currently pursuing his PhD from CSIR-Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh, India. He was awarded DST-INSPIRE Fellowship for pursuing PhD, sponsored by the Department of Science and Technology (DST), Government of India, 2013.

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