**STUDY ON THE FUNCTIONAL ROLE OF FISH TRANSIENT RECEPTOR POTENTIAL MELASTATINE 2 CHANNEL**

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***Abstract***

Pollutants such as reactive oxygen or nitrogen spices (ROS or RNS) in wastewater released into the aquatic environment cause serious impacts on fish health. In different animal species, transient receptor potential (TRP) proteins have been well known to form sensor cation channels for detection of a variety of environmental stimulants. To elucidate sensing mechanisms that allow fish to avoid pollutants in the environment, we here characterize the zebrafish (*Danio rerio*) homologue of TRPM2, whose mammalian homologue has been reported to show prominent sensitivity to ROS, especially to hydrogen peroxide (H2O2). Our results showed that the zebrafish TRPM2 (drTRPM2) protein forms a Ca2+-permeable cation channel activated by H2O2. Strikingly, in contrast to mammalian TRPM2, drTRPM2 responds to nitric oxide (NO) and nitrite (NO2-). This distinctive RNS sensitivity of drTRPM2 channels is mediated by cooperative action of ADP ribose (ADPR) and cGMP-dependent protein kinase (PKG), and sensitivity is mediated mainly by ADPR. In addition, homozygous TRPM2 knock out zebrafish generated using the CRISPR/Cas9 system fails to show repellent behaviors against H2O2 and NO. Thus, TRPM2 channel plays an important role for fish to sense to the polluted environment.

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