

# Zebrafish model gives new insight on autism spectrum disorder

27 May 2015



Autism Spectrum Disorder (ASD) is a neurological condition that affects approximately two percent of people around the world. Although several genes have been linked to multiple concurring conditions of ASD, the process that explains how specific genetic variants lead to behaviors characteristic of the disorder remains elusive.

Now, researchers are utilizing animal models to understand how dysfunction of either of two [genes](#) associated with ASD, SYNGAP1 and SHANK 3, contributes to risk in ASD. The new findings pinpoint the actual place and time where these genes exert influence in brain development and function. The findings are published in the journal *Human Molecular Genetics*.

"The overall goal of our study was to generate and directly compare two zebrafish models of ASD, to gain an in vivo perspective on how ASD genetic variants impact neural circuit development in embryos," said Julia E. Dallman, assistant professor of biology at the University of Miami (UM) College of Arts and Sciences and lead

investigator of the study. "Our work begins to address a major gap in our current understanding of ASD."

The findings show that disrupting the expression or "knocking down" either SYNGAP1 or SHANK 3 genes affects [early brain development](#) in the mid and hindbrain regions and results in hyper-excitable behaviors.

"It is well known that genetics plays a significant role in ASD risk and that many genes are involved, but the exact nature of their involvement is not well understood," said Margaret A. Pericak-Vance, director of the John P. Hussman Institute for Human Genomics, the Dr. John T. Macdonald Foundation Professor of Human Genetics, at the UM Miller School of Medicine and co-author of the study. "The implications of the present study are important as it helps us understand how two ASD related genes, SHANK3 and SYNGAP1, contribute to the development of the disorder."

The study is titled "Two knockdown models of the autism genes SYNGAP1 and SHANK3 produce similar behavioral phenotypes associated with embryonic disruptions of brain morphogenesis." In contrast to previous studies of ASD-linked genes in humans and mice, the current study is conducted in developing zebrafish, because zebrafish embryos are transparent organisms that develop outside the mother, thus allowing the researchers to observe early [brain development](#) in the fish.

The researchers chose to analyze SYNGAP1 and SHANK3 orthologs—genes in different species that have a common ancestor and maintain the same function, since embryonic functions of these ASD-linked genes are unknown.

The study utilized three groups of fish. In two of the groups, the expression of either SYNGAP 1 or SHANK 3 genes was knocked down by injecting a molecule that specifically targets each gene. The

third was also injected with a similar molecule, but with no match in the zebrafish genome, so it functioned as a control group. The behavior of larvae in all groups was analyzed by studying their escape responses in the presence of a stimulus.

The experiments showed that while control larvae swam away from the stimulus, the knock-down larvae had unproductive escape responses, as well as significantly reduced swimming velocities. Moreover, a subset of the knock-down larvae exhibited spontaneous seizure-like behaviors, and there were significant changes in the brain structure of these larvae, indicative of delayed development.

Together these findings support the emerging opinion that mutations of specific ASD-related genes disrupt early embryogenesis and that these early disruptions play a key role in the development of the disorder.

The team is now working to determine exactly how early developmental deficits impact later behaviors. In the long-term, they hope to use SYNGAP1 and SHANK3 zebrafish models for drug screening, to identify environmental risk factors and test potential therapies for ASD.

**More information:** *Human Molecular Genetics*, [hmg.oxfordjournals.org/content ... mg.ddv138.full#aff-2](https://hmg.oxfordjournals.org/content/31/12/mg.ddv138.full#aff-2)

Provided by University of Miami

APA citation: Zebrafish model gives new insight on autism spectrum disorder (2015, May 27) retrieved 31 July 2022 from <https://medicalxpress.com/news/2015-05-zebrafish-insight-autism-spectrum-disorder.html>

*This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.*