Thomas Edlinger
Public Relations and Event Management

Medical University of Graz
Neue Stiftingtalstraße 6
8010 Graz
thomas.edlinger@medunigraz.at

Press release
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From gene to behavior: What we can learn from aggressive zebrafish

Graz, 7 July 2025: Aggression is a complex behavior dependent on numerous factors such as personal experiences, upbringing, social context, personality and genetics. Florian Reichmann and his team at the Med Uni Graz Division of Pharmacology conduct research on how it is influenced by genetics. With the help of genetically modified fish, they want to obtain insight into the origin of behaviors and possibly draw conclusions about human behavior.

The zebrafish as a model

The test model of Florian Reichmann's working group is the zebrafish. No more than five centimeters long, this small and popular aquarium fish in the carp family has increasingly been used as a test organism in research. Around 70 percent of zebrafish DNA have orthologs (i.e., genes with a similar function) compared to the human genome; this number even approaches 82 percent in terms of disease-related genes. Other unusual features of the zebrafish are its quick development—its heart beats just 24 hours after fertilization—, its great fertility with each couple producing several hundred offspring and its nearly complete transparency in the larval stage, which opens up a variety of possibilities for in vivo microscopy.

For their research involving the zebrafish model, Floran Reichmann and his team have studied the zebrafish gene Irrtm4l1. It is orthologous to the human gene LRRTM4. The latter "codes a protein that plays a critical role in the development of synapses (junctions between neurons) and their adequate function," explains Reichmann. Polymorphisms, i.e., changes or errors in this gene, have been associated with aggression problems in children, autism spectrum disorders and Tourette's syndrome. In order to investigate this relationship more closely, the researchers bred zebrafish whose ortholog Irrtm4l1 gene has been "turned off." Finally, they meticulously analyzed the behavior of the fish and molecular changes in their brains.

Peaceful fish

A glimpse in the aquarium yielded interesting findings with regard to the genetically modified fish. The research group was able to establish that the transgenic fish were generally less aggressive. This suggests that this gene plays an important role in the development of aggression. The reason for reduced aggressivity might be increased timidity, yet it probably stems from a changed perception of "enemies" and/or a decreased desire to attack. A large number of changes were detected in the brain using omics technologies and targeted

neurotransmitter measurements. Of special interest are both a higher dopamine turnover—dopamine is a neurotransmitter that has been associated with aggression in earlier studies—and reduced methyl vanillate concentrations. Methyl vanillate is a derivative of vanillin, which has been associated with neuroprotective and antioxidative effects.

LRRTM4 as a target

From a translational perspective, research on zebrafish has shown that LRRTM4 may indeed play an important role in human behavior. "For example, a method might be found for treating excessive aggression or anxiety disorders within the framework of neuropsychiatric diseases," explains Reichmann. However, further research on the development of suitable active substances and the confirmation of the effects in other test organisms are required.

Link to the study:
https://onlinelibrary.wiley.com/doi/10.1111/apha.70042

Further information and contact

Florian Reichmann
Division of Pharmacology
Research Field Neuroscience
Medical University of Graz
Tel.: +43 316 385 74122
Email: florian.reichmann@medunigraz.at

Profile: Florian Reichmann
Florian Reichmann is a tenure track professor in the Division of Pharmacology at the Otto Loewi Research Center and is the head of a Medical University of Graz research group in behavioral neuropharmacology. The pharmacologist has many years of experience in behavioral research and experimental neuropharmacology. He focuses on exploring the genetic components of pathological behavioral changes as well as the microbiota-gut-brain axis and analyzing interactions between genetic and nongenetic factors. The goal of his research is to find novel therapeutic targets for treating pathological behavioral changes within the framework of psychiatric, neurological and chronic inflammatory disease.