Autism-related gene *mbd5* disruption impairs iron homeostasis in zebrafish

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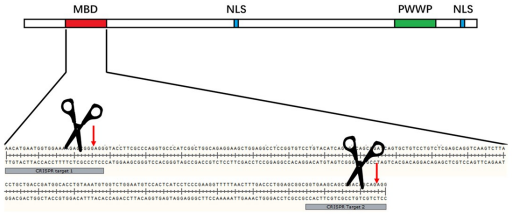
Introduction

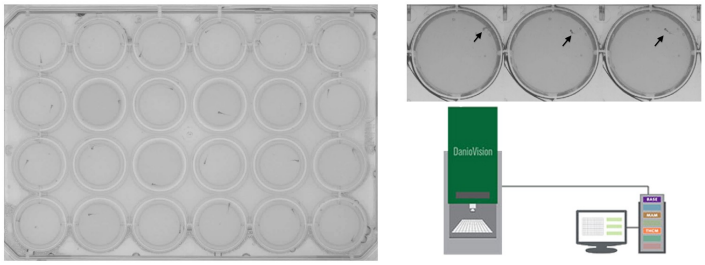
- ***MBD5*** **is only locus of 2q23.1 microdeletion syndrome, whose phenotypic features include autism, seizures, sleep disturbance, and craniofacial abnormalities.**
- ***MBD5*** **also regulates iron metabolism, however, the link between iron homeostasis and autism spectrum disorder remains poorly known.**
- **Zebrafish, a model for neuropsychiatric disorders, can be bred in large groups, is easy for genetic manipulation and drug screening, with relatively simple behavior to observe, and transparency that allows live imaging.**

Experimental methods

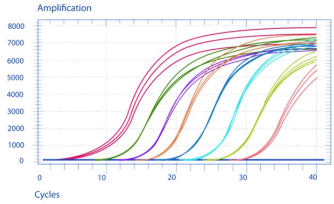
Using CRISPR/Cas9 system to construct zebrafish mutants.



High-throughput Behavior test—using Noldus DanioVision® system to record the behavior and track the movement by Ethovision® software.



Analyze the expression of iron metabolism-related genes by RT-PCR.



Acknowledgement & references

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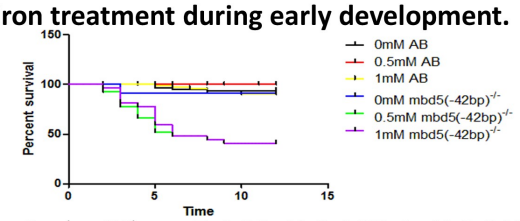
References:

Mullegama, Sureni V., et al. "Reciprocal deletion and duplication at 2q23.1 indicates a role for *MBD5* in autism spectrum disorder." *European Journal of Human Genetics* 22.1 (2014): 57-63.
Stewart, Adam Michael, et al. "Developing zebrafish models of autism spectrum disorder (ASD)." *Progress in Neuro-psychopharmacology & Biological Psychiatry* (2014): 27-36.
Tao, Yunlong, et al. "*MBD5* regulates iron metabolism via methylation - independent genomic targeting of Fth1 through KAT2A in mice." *British Journal of Haematology* 166.2 (2014): 279-291.

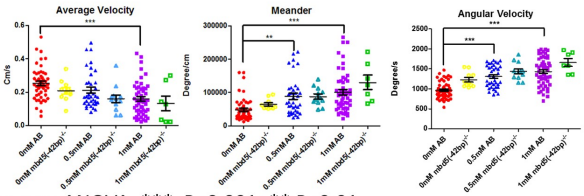
Results

1. **Zebrafish *mbd5* mutants are more susceptible to iron treatment during early development.**



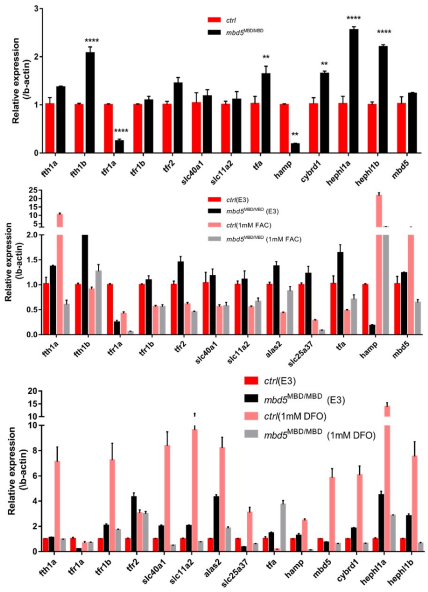
Gehan-Breslow-Wilcoxon Test, 0.5mM, P<0.001; 1mM, P<0.001.

2. **Iron treatment fails to induce behavior changes in *mbd5* mutants.**



One-way ANOVA, *** P<0.001; ** P<0.01.

3. **The expression of iron metabolism-related genes are dysregulated in *mbd5* mutants and are aggravated with iron or iron chelator treatment.**



One-way ANOVA, *** P<0.001; ** P<0.01.

Discussion

- **MBD5 may play a role in response to environmental iron changes and may directly regulate the expression of iron metabolism-related genes.**
- **Iron metabolism dysfunction caused by *MBD5* mutation may not be the cause for autism.**
- **Future experiments like ChIP-seq and tissue elements analysis will provide more evidences.**