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A functional evidence for *ATF7IP* association with human intellectual disabilities

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Background

Intellectual disability (ID) is considered a multifactorial disorder with a high prevalence that compels considerable burdens on societies. A genome-wide association study (GWAS) on Iranian ID families reported an association of a novel genetic mutation in the *ATF7IP* gene. Although this demonstration has diagnostic importance, its functional role needs to be scrutinized. *Drosophila melanogaster* is a unique and well-known model organism to perform such functional investigations as its tiny brain resembles a high level of neurogenetics and neurofunctional identities to the human brain.

Materials and Methods

The Gal4/UAS system is a highly applicable tool in *Drosophila* genetics that offers over-expression and/or silencing of a particular gene in a time- and tissue-specific manner. Therefore, the RNAi approach was employed to knock down the *wde* gene, fly ortholog to *ATF7IP*, in flies' brain. Following confirmation of *wde* down-regulation, its pathologic effects on the structure and function of neurons were assessed by brain microscopy and validated behavioral assays including olfactory conditioning, and courtship conditioning learning and memories.

Results

Based on huge functional similarities between the selected *ATF7IP* gene and its orthologs in *Drosophila melanogaster*, down-regulation of the *wde* gene led to neuronal dysfunction and induction of some sort of ID-like symptoms in flies such as

- Adult olfactory memory deficits.
- Impaired courtship conditioning learning and
- Abnormal MBs structure

Conclusion

Since the transgenic Drosophila with brain-specific down-regulation for the selected gene display abnormalities in neuronal structure and functions, and memory performance then it can be considered as evidence for the statement on the association of observed genetic alterations and familial ID in the Iranian population.

References

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