CHRD 2024: Abstract Submission Form

Presenter Name
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Presenter Status
PhD Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Pathogenic ELFN1 variants in mGluR4 function

Background
In the brain, excitatory neurotransmitter glutamate activates G-protein coupled receptors (GPCRs) termed metabotropic glutamate receptors (mGluRs). These receptors are considered as highly viable avenues for drug design for neurodevelopmental disorders (NDDs). Recently, we have identified that group III mGluRs are trans-synaptically regulated by synaptic adhesion molecules (SAMs). Extracellular leucine rich fibronectin type III domain 1 (ELFN1) is a type of SAM which engages group III mGluRs trans-synaptically. Recently, disease causing human ELFN1 gene variants have been identified developing diverse NDDs.

Objective
In this study, we aim to evaluate the consequence of ELFN1 variants on mGluR4 function guiding novel therapeutic strategies for ELFN1-mediated NDDs.

Methods
To accurately assess the impact of ELFN1 mutations, mammalian expression plasmid vector pcDNA was used to insert various human ELFN1 pathogenic mutations. Wildtype and the mutated plasmids were transfected into the prototypical cell line of GPCR pharmacology: HEK293. After harvesting cells, we performed expression analysis via Western blotting and co-immunoprecipitation experiments to assess the expression levels of the ELFN1 variants and their trans-cellular interactions with mGluR4, respectively.

Results
Western Blotting showed the expression of the mutated variants of ELFN1. Subsequently, co-immunoprecipitation demonstrated that wildtype and intracellular mutated ELFN1 interact properly with the mGluR4 suggesting mGluR4-independent mechanism; however, no interaction was observed in extracellular ELFN1 mutation which ultimately suggests an mGluR4-dependent mechanism in the pathogenesis of NDDs.

Conclusion
This is ongoing research and provided here some preliminary observations. A holistic approach would provide an early and unique description of molecular consequences of pathogenic these ELFN1 variants.

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No

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