

Presenting Author Name

Simrat Dhaliwal

Presenting Author Category

Masters Student

Research Category

Basic Science

Abstract Title

Evaluating the Modulatory Activity and Binding Capacity of ELFN1 on mGluR8 In Trans

Background

Approximately 15% of children and adolescents worldwide are affected by neurodevelopmental diseases (NDD). G protein-coupled receptors (GPCRs) are essential in the proper regulation of synaptic transmission; therefore, their pathways act as promising targets for pharmacological intervention with GPCRs already being targeted by 35% of FDA approved pharmaceuticals. Recent studies on GPCR extracellular binding partners highlight the concerning limited understanding of GPCR synaptic neurobiology. Interestingly, one of these extracellular binding partners is a synaptic adhesion molecule called extracellular leucine-rich repeat and fibronectin type-III domain-containing protein 1 (ELFN1), which can modulate a subset of GPCRs- group 3 metabotropic glutamate receptors (mGluRs). Mutations within ELFN1 have been linked to various NDDs including the general etiology of epilepsy, ADHD, and autism.

Objective

This study aims to determine the trans-synaptic consequence of ELFN1 on mGluR8 binding in trans.

Methods

Co-immunoprecipitation experiments were conducted by co-culturing HEK293 cells transfected with mGluR8-HA and wildtype ELFN1 or clinically pathogenic ELFN1 variants. Binding capacity was analysed via western blotting and densitometry. The Transcellular GPCR Signalling Assay Platform was utilized to assess mGluR8 activity using ONE-GO biosensor readouts.

Results

In comparison to reference ELFN1, the extracellular ELFN1 variant exhibited significant reduction in its binding capacity with mGluR8, suggesting an mGluR8-dependent pathogenic mechanism. Furthermore, reference ELFN1 negatively regulated mGluR8 activity while the extracellular variant displayed disrupted modulatory activity of mGluR8.

Conclusion

The disruption of mGluR8-ELFN1 complex sheds light on potential therapeutic strategies for patients harboring this variant.

Authors

Name	Role	Profession
Simrat Dhaliwal	Presenting Author	Graduate
Henry Dunn	Co Author	Assistant Professor