CHRD 2024: Abstract Submission Form

Presenter Name
Sarah Cameron

Presenter Status
Undergraduate Students

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
L1 syndrome-causing L1CAM in transcomplex with mGluR5

Background
L1 syndrome is a severe neurodevelopmental disorder that causes intellectual, physical, and developmental birth defects. It is caused by disruptions in the synaptic adhesion molecule L1CAM, and this molecule was recently found to interact with mGluR5. mGluR5 is a well-established drug target for neurological disorders, so mGluR5 in trans-complex with L1CAM may have major implications in the etiology of L1 syndrome.

Objective
Our objective is to determine whether there is a transcellular interaction between L1CAM and mGluR5.

Methods
Using public mass spectrometry data, we highlighted L1CAM as a potential binding partner of mGluR5. Co-immunoprecipitation experiments were conducted to detect binding of mGluR5 with full-length L1CAM and the ectodomain of L1CAM. This was done by transfecting L1CAM, L1CAM-Fc ectodomain, and mGluR5 DNA into HEK cells. Cells were lysed and proteins were isolated. Lysate and co-immunoprecipitation samples were made and run through the Western blot process. Data is analyzed via the presence or absence of the proteins.

Results
Co-immunoprecipitation experiments showed that mGluR5 binds to full-length L1CAM as well as the ectodomain of L1CAM, verifying that the interaction occurs transcellularly. This is seen through qualitative western blot data. The full-length L1CAM experiment shows that full-length L1CAM binds specifically to mGluR5, and does not bind randomly as there is no binding in the control lane. The L1CAM ectodomain experiment shows that mGluR5 binds specifically to the extracellular portion of L1CAM, and does not bind randomly as there is no binding in the control lane.

Conclusion
Verification of L1CAM-mGluR5 transcellular complexes leads to new hypotheses, including whether L1CAM modulates mGluR5 pharmacology, and whether pathogenic mutations for L1 syndrome in L1CAM disrupt interactions with mGluR5. This research will further our understanding of L1 syndrome, and possibly other neurological disorders associated with mGluR5.

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Authors

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