



July 2024 Research Roundtable Summary

Featuring guest speakers Dr. Lee and Dr. Rubio

Chelsea's Hope hosted their quarterly Virtual Research Roundtable on July 11th 2024, with more than 60 attendees representing the research, clinical, and patient communities. Our guest speakers were Dr. Bumwhee Lee from GenixCure and Dr. Teresa Rubio from Universidad Europea Valencia. We also received a progress report on the planned ION283 Safety Study from Dr. Berge Minassian at University of Texas Southwestern Medical Center.

Dr. Bumwhee Lee has worked in the neuroscience field for five years, specializing in AAV gene therapy research at GenixCure in South Korea. Dr. Lee presented proof-of-concept data for gene therapy to replace the EPM2A gene that codes for the protein laforin, which recently received Orphan Drug Designation from the FDA. GenixCure optimized an AAV9 viral delivery system to reduce adverse immune response and tested the therapy in a mouse model. Mice were treated with the gene therapy at 4 months of age and the therapeutic impact analyzed at 9 months of age. Their analyses confirmed broad expression of laforin in the neurons of mice, reduced expression of neuroinflammation markers, and improved motor function using a rotarod test. The next step would be testing dosage response in the mouse model.

Our second guest speaker was Dr. Teresa Rubio, a collaborator with the Sanz Lab at the Universidad Europea Valencia in Spain. Dr. Rubio shared data from a recent publication titled, "Beneficial Effect of Fingolimod in a Lafora Disease Mouse Model by Preventing Reactive Astrogliosis-Derived Neuroinflammation and Brain Infiltration of T-lymphocytes." In this study, they measured neuroinflammation in malin knockout (MKO) mice and noted a significant increase in the CXCL10 neuroinflammation marker, which is known to increase with age and be primarily expressed in astrocytes. When MKO mice were treated with fingolimod, a drug proven to reduce infiltration of immune cells, the number of CD4 and CD8 cells decreased and fewer reactive astrocytes were observed. While treatment with the drug did not decrease Lafora body accumulation, a series of behavioral tests suggest that the decline of cognitive and motor skills was slowed in MKO mice treated with fingolimod. Future studies will examine potential synergistic effects with metformin and other neuroprotective drugs.

After our research presentations, Dr. Berge Minassian gave a brief progress report on the ION283 Safety Study submission that he announced at our last Research Roundtable. Dr. Minassian shared that the additional data requested by the FDA in May had been collected and submitted. They are now waiting for the FDA to review this new data. Additionally, Dr. Minassian shared that the FDA requested that the study be

restricted to patients ages 12-18. For the most up-to-date information on the Safety Study, please visit our webpage: <https://chelseashope.org/safety-study/>

Thank you for reading our Roundtable Summary and please do not hesitate to contact our Science Director, Dr. Kit Donohue, if you have any questions or suggestions: katherine@chelseashope.org.