GM604 – A Multiple-Target Regulator that Provides a Novel Therapeutic Strategy for Treatment of ALS and Other Neurodegenerative Diseases

Markindy K1,2, Michael L. Swindell1, Krzysztof Bojanowski3, Paul Lippincott1, Robert Bowser1, Raphael Nir1, Marisa Westlin1, Tony Shum1, Raymond Chan1, Dorothy Ko4
1Department of Pharmaceutical Sciences, College of Pharmacy, University of South Florida, Tampa, FL, USA. 3James A. Haley VAMC, Tampa, FL, USA. 4Ohio University, Heritage College of Osteopathic Medicine, Athens, OH, USA. 2Sunny Biodesign Inc., Santa Clara, CA, USA. 5Villanova University, Villanova, PA, USA. 6Iron Horse Diagnostics Inc., Scottsdale, AZ, USA. 7SBB Sciences, Natick, MA. 8Genervon Biopharmaceuticals, LLC. CS, Pasadena, CA, USA.

Abstract

The genome-wide analysis of RNA-seq data from genetically engineered mouse models of ALS (104) through Genervon’s Phase 1 clinical study (6) demonstrated that GM6 delayed disease onset and reduced mortality in both models. In the present study, we further evaluate the effects of GM6 on the human disease model, and consider the potential for GM6 to provide a novel therapeutic strategy for ALS patients and other neurodegenerative diseases. We initially conducted a neuroprotective in vitro experiment in which SH-SY5Y cells were treated with GM6 for varying lengths of time (24-48 hours), with the goal of identifying potential gene targets. GM6 was found to increase the expression of genes known to be associated with neuroprotection, synaptic transmission, and neurogenesis, and to decrease the expression of genes associated with neurodegeneration. These results suggest that GM6 has the potential to provide novel therapeutic strategies for ALS and other neurodegenerative diseases.

Methods

1. Neuroprotection on rat cortical neurons from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).
2. Neuroprotection of human astrocytes from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).
3. Neuroprotection of human microvascular endothelial cells from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).

Results

1. Neuroprotection of rat cortical neurons from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).
2. Neuroprotection of human astrocytes from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).
3. Neuroprotection of human microvascular endothelial cells from excitotoxic injury using high levels in the adult mouse model of amyotrophic lateral sclerosis (ALS).

Conclusions

We have shown that GM6 promotes neuroprotection against toxic factors contained in CNS microvascular tissue and is a potential therapeutic agent for the treatment of ALS and other neurodegenerative diseases.