Wake Forest School of Medicine

Department of Neurobiology and Anatomy
ALS Translational Science Unit

Progress Report: Blazeman Foundation – October 7, 2014

Project Title: Administration of Hsp70 maintains muscle innervation in the SOD1 mouse- a new therapeutic approach?

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Institution: Wake Forest School of Medicine

Project Summary:

Researchers at Wake Forest School of Medicine have found a new treatment that may delay the onset of symptoms and increase the lifespan for those who are afflicted with ALS, or Lou Gehrig's disease. The researchers have determined that injections of a particular type of protein called heat shock protein (Hsp) 70 may benefit ALS suffers. The study was conducted in the mutant SOD1 mouse model of ALS. When the mice were given treatments of Hsp70, their survival was increased. This study focused on protecting the motor neurons in the mice that had ALS. The injected protein was not detected in the nervous system of the mice. Rather, this treatment appeared to work where the neurons and muscles contact each other. When the neurons and muscles loose contact, muscle weakness occurs, the prominent symptom of ALS. In a second study, the group found that the contact between neurons and muscle was maintained much longer in treated mice as compared to untreated mice. While these studies have shown positive signs, researchers caution that many more studies are needed before they can begin to conduct clinical trials in people. The group has a smaller fragment of the protein that also shown positive effects and is currently being more intensely tested. The group is determining the best way to efficiently produce the proteins to assure they will function properly. This is the first step to develop the protocols for protein production and develop GMP large-scale production strategies that will facilitate IND application and clinical trials. With support from the Blazeman Foundation, Wake Forrest School of Medicine is the only medical center that is engaged in researching this potential ALS treatment.

Thus far we have:

1. Developed protein production, isolation and purification protocols that allow us to isolate recombinant Hsp70 and its substrate binding domain derivative (SBD) with greater than 95% purity.
2. We have begun testing in the SOD1 mouse model of ALS to confirm and extend our previous results indicating that administration of the protein delays early denervation of neuromuscular junctions.
3. Begun to work with Wake Forest Innovations to develop best strategies to move forward toward Phase 1/2 clinical trials.

During the upcoming months we will:

1. Continue to modify our purification protocols to increase the amount of protein we collect without compromising purity. Our goal is to increase yield by three fold.
2. Complete initial animal studies using the dose of Hsp70 and the derivative we originally reported to be effective.
3. Begin dose response studies in the mouse model.
4. Begin to develop a reliable protocol that will allow us to confirm that administered protein reaches it's predicted target, i.e., muscle.
5. Work closely with the Blazeman Foundation, WFSM Development Office and WF Innovations to determine best strategies moving forward.