

September 1, 2016

Dear Mary Ann, Bob, and all Blazeman Warriors:

As you are aware, our lab at Wake Forest has determined that injections of a particular type of protein called heat shock protein (Hsp) 70 may benefit ALS sufferers. Our original study was conducted in a mouse model of ALS. When the mice were given treatments of Hsp70, their survival was increased. This treatment appeared to work where the neurons and muscles contact each other. When the neurons and muscles lose contact, muscle weakness occurs, the prominent symptom of ALS. In a second study, we found that the contact between neurons and muscle was maintained much longer in treated mice as compared to untreated mice. With limited funding, the future of Hsp70 in ALS was limited. However, with support from the Blazeman Foundation for the past several years, we have developed a way to reliably and reproducibly produce the protein. This crucial step now enables us to continue to move forward to finding potential treatments for ALS.

Recently, we received the results from an analysis of purity of our protein. We are very excited that the results that our protein preparations contain our protein, and little of anything else. In addition, our results with activity assays indicate that our in house protein's activity is 30% greater than commercially available protein, or protein we made initially before making final modifications to the production protocol. So all together, it looks like we have made what we set out to do. Over the next few months, we should be able to complete our animal studies. Our preliminary results are encouraging, but because these are blinded studies, we will not have final results until all animals have been treated and experimental codes revealed. With additional positive results, our ALS scientists and clinicians will begin to design initial clinical trials in patients.

We want everyone to know that contributions to research do so much more than pay for test tubes and beakers. Supporting research allows us to:

- Conduct studies to prove or disprove proposed ideas
- Recruit scientists with complementary expertise, who together can collaborate and develop new potential therapies
- Train the future scientists who will find a cure.

The Blazeman Support of the Hsp70 project is a perfect example. Funding from the foundation allowed us to bring on Mac Robinson, who as a graduate student in our lab developed the first protocol we used to produce recombinant protein. When we received the Blazeman Funding, Mac re-joined us as a junior faculty member and was essential to developing the protocols we now use to produce Hsp70. Interestingly, Mac completed his postdoctoral training in our Human Genomics and Personalized Medicine Center where he studied IL-6 signaling in asthma. Having Mac back in the group led to collaboration with the ALS research group and the Human Genomics group where our team is now exploring a precision medicine approach for treating certain patients with ALS. Although the sequence of symptoms and progression varies among ALS patients, all patients lose muscle mass and have difficulty breathing. When muscles

atrophy as happens in ALS, a protein called interleukin-6 (IL-6) is produced. While IL-6 has role in inflammation, it also has a role in motor neuron survival. Therefore, we believe it may play a complex role in ALS. Our project is to investigate if IL-6 signaling changes as the disease progresses. A percentage of the population has a genetic difference in the receptor for IL-6 and has enhanced signaling. Knowing which patients have this genetic difference will allow physicians to identify patients for whom IL-6 blocking-therapies will be most effective. The project includes an MD/PhD Student who is well on her way to becoming a future ALS investigator.

On behalf of all members of our ALS Center, we continue to express our gratitude to the Blazeman Foundation - because of this support we continue as Jon asked, we choose to "Believe...Pick a stronger word than Hope...Cure"