UNC DEPARTMENT OF NEUROLOGY

October 2nd, 2022

To whom it may concern:

My name is Todd Cohen, I run a laboratory located in the Department of Neurology at University of North Carolina-Chapel Hill, where we have built a program studying how aggregated proteins accumulate in various tissues and eventually cause degeneration. Our goal is to block this process with therapeutics and gene therapies to generate healthier cells and alleviate symptoms of protein aggregation diseases that affect the brain, the heart, and skeletal muscle. Over the last 15 years, our lab has built a track record in publishing impactful papers that demonstrate that demonstrate how aggregates affect muscle and brain similarly.

Because we have spent much effort studying the protein TDP-43, we have learned that many diseases show overlapping similarities. In particular, TDP-43 is the aggregated protein in neurodegenerative disease such as frontotemporal degeneration (FTD) and amyotrophic lateral sclerosis (ALS), but many do not appreciate that TDP-43 also accumulates in most instances of sporadic inclusion body myositis (sIBM). Therefore, the emerging belief is that FTD, ALS, and sIBM lie within a common spectrum of disorders known as TDP-43 proteinopathies. In fact, in our lab we routinely refer to sIBM as "ALS of the muscle". This is an important point since, in my opinion, these different clinical entities should be viewed along a continual spectrum of diseases that are all due impairments in processing the TDP-43 aggregates. The assumption is that, since the degeneration that one sees in these diseases is similar, then if one develops therapies against FTD and ALS, they could be effective against sIBM as well.

There are many overlaps between sIBM and ALS. Both sIBM and ALS patients can develop TDP-43 aggregates in muscle. These patients can have substantial clinical overlap and sometimes present with both syndromes. Both are profoundly debilitating and result in progressive muscle weakness. Our lab has actually demonstrated that TDP-43 aggregates can be generated in mouse muscles and that these aggregates look identical to those seen in ALS patients. Finally, both disorders are thought to have a poorly understood environmental component including exposures to toxins, herbicides, fungicides, and other drivers of inflammation and/or protein aggregation that results in TDP-43 pathology. Military veterans represent a population at high risk since they are exposed to many of these toxic environmental agents. Our lab is now trying to identify many of these factors, with publications forthcoming.

I hope you will agree that sIBM and ALS should be considered very similar disabilities that we and others have documented in the literature. Veterans with sIBM should be granted much deserved disability benefits due to this overlap. Don't hesitate to contact me with any further questions about this important matter.

Sincerely,

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