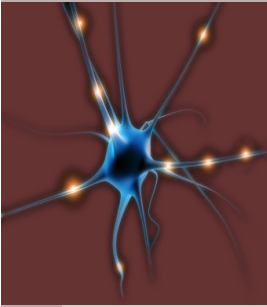


Winter,  
2016-2017



WASHINGTON UNIVERSITY DEPARTMENT OF NEUROLOGY

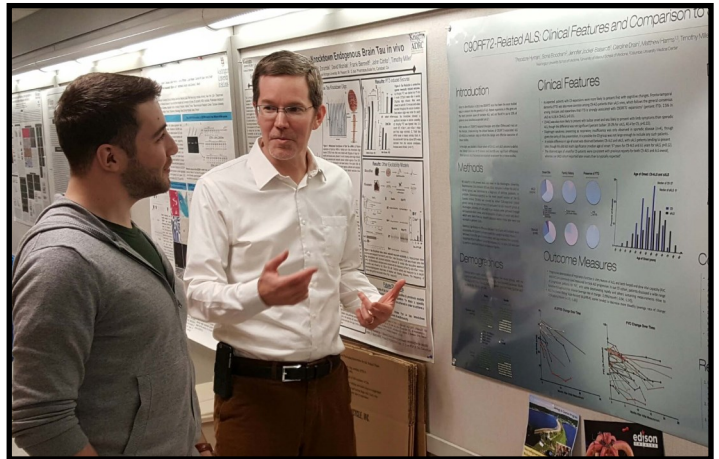
# ALS Research Update

## A Study of C9ORF72-related ALS

About 5-10% of patients with ALS have an abnormal expansion in the gene C9ORF72. Therapies are currently being developed for this particular subset of ALS patients. As these therapies are being considered, it is important to fully understand the details and characteristics of ALS in this particular patient population. Washington University has launched a natural history and biomarkers study including eight sites across the United States and Europe to answer this important question by enrolling patients with the C9ORF72 gene mutation in this study.

Another way to understand clinical details in C9ORF72 ALS is to examine the past clinical records for pa-

tients with this mutation who have been seen in the Washington University ALS clinic. This past summer, we completed this type of retrospective analysis for 49 patients and presented our findings at the annual meeting of the Northeast ALS Consortium in Tampa, Florida. This first look at the disease characteristics of C9ORF72 is currently being incorporated into planning for clinical trials, specifically for C9ORF72 ALS. Therefore, the valuable clinical data we collect from current ALS patients who visit Washington University has a direct benefit for therapeutic clinical trials and patients with ALS in the future. To obtain additional information, please call 314-362-6159 or email: [neuroclinicalstudies@neuro.wustl.edu](mailto:neuroclinicalstudies@neuro.wustl.edu)



*Timothy Miller, MD, PhD, and Ted Hyman, Research Technician, discuss the C9ORF72 retrospective study which will be important for designing upcoming clinical trials.*

## Development of an Imaging Tracer for Protein Aggregates in ALS and FTL D

Aggregates of a protein called TDP-43 are a characteristic hallmark of ALS and frontotemporal lobe degeneration (FTLD). There have been many hypotheses regarding the role of TDP-43 in causing disease. In order to understand the protein's disease-causing role, an accurate and reliable method to detect and measure TDP-43 aggregates in the human body is necessary.

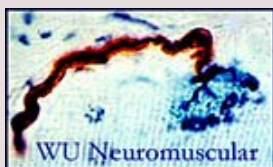
Positron emission tomography (PET) tracers are widely used in numerous diseases as medical and research tools. These tracers are composed of labeled molecules that are introduced into the body and emit signals that show the location of the proteins of interest via computer analysis after the patient undergoes a PET/CT scan. Development of a PET tracer for TDP-43 aggregates would allow researchers to visualize and study TDP-43 protein in ALS and FTLD patients. This would enable more accurate clinical diagnoses as well as a method to monitor the effectiveness of new therapies on TDP-43.

Drs. Timothy Miller, Paul Kotzbauer, Vijay Sharma, and Nigel Cairns of Washington University, as well as Dr. Yuna Ayala of Saint Louis University, were recently awarded a research grant from ALS Finding a Cure and the ALS Association to generate a PET tracer for TDP-43 aggregates. The researchers have established methods to identify and optimize potential PET tracer compounds and are well-positioned to further develop these molecules for human use. With the combined experience and expertise of this collaborative team, it is likely that the ALS field will reap the benefits of a working TDP-43 PET tracer within the coming years.

## Collaboration with Ilya Gertsman

The Miller Lab is collaborating with colleagues at University of California-San Diego to explore a new clue to the puzzle of genetically inherited ALS. SOD1 is one of the most common genes involved in inherited ALS. Dr. Ilya Gertsman, a researcher at UCSD, found a new marker for ALS: a small fragment of SOD1 flowing through the space surrounding the spinal cord. As is often the case in science, this discovery raised more questions. What produces this SOD1 protein fragment? How does the protein make its way out of the spinal cord and into the surrounding fluid? The Miller Lab is working with Dr. Gertsman to answer these riddles, providing samples and expertise needed to work out exactly how this protein fragment relates to ALS.

The first set of data we have generated through this collaboration is fascinating. Not only does this protein fragment build up in SOD1-related ALS, but a similar (though less drastic) change is seen in ALS cases that do not run in families. Washington University already has an effective SOD1-targeting drug in development in animal models and the drug has been shown to be safe in humans with ALS. The only limitation, as of now, is the limited scope of the treatment—as it is only expected to help the 1-2% of ALS patients with SOD1 mutations. Proof that SOD1 is involved in causing or worsening non-genetic ALS would drastically expand the use of this drug, and pave the way for the first ALS-specific therapy in more than two decades.



<http://millerlab.wustl.edu/>  
<http://neuromuscular.wustl.edu/>

***We gratefully acknowledge the support of the following organizations:***

Hope Center for Neurological Disorders

Project 5 for ALS

Muscular Dystrophy Association

The ALS Association

NEALS - Northeast ALS Consortium

National Institutes of Health

Robert Packard Center for ALS

Target ALS

University of Missouri Spinal Cord Injury and Disease Research Program

Ionis Pharmaceuticals

Biogen Idec MA Inc.

## Welcome, Amber!

Amber Malcolm joined the Neuromuscular Division in October, 2016. Her role is two-fold: providing clinical care for persons with ALS and helping expand ALS research opportunities at Washington University.

Clinical care of ALS patients includes meeting with them in the Thursday clinic as well as providing a central point of contact for patients as they deal with the challenges of ALS. Amber's research responsibilities include assessing patients and reviewing medical records as well as performing measurements for many different ALS studies. The goal is to increase the number of observational and interventional trials while providing comprehensive clinical care.



**Amber Malcolm MSN,  
RN, ACNP-BC  
Nurse Practitioner**

## *How can you help The Miller Lab?*

### *Charitable donations support ALS research*

For contributions to the Washington University ALS program, please contact Zach Silvers, Senior Director of Development, at 314-935-3498 or email [zsilvers@wustl.edu](mailto:zsilvers@wustl.edu). Those who wish to send a check should write it payable to Washington University. In the memo section, please indicate the gift is to "ALS Research Support Fund."

Checks should be sent to:

Medical Alumni and Development, Attn: Zach Silvers  
7425 Forsyth Blvd., Suite 2100, St. Louis, MO 63105



***Staff from the Washington University School of Medicine Department of Neurology teamed up at Forest Park on June 25th, 2016 to support the Walk to Defeat ALS.***