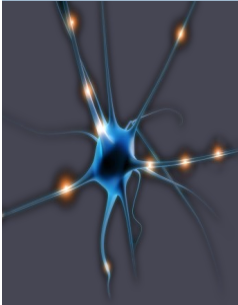


Fall,  
2018



WASHINGTON UNIVERSITY DEPARTMENT OF NEUROLOGY

# ALS Research Update

## Dr. Timothy Miller Receives Sheila Essey Award

The ALS Association, in partnership with the American Academy of Neurology and the American Brain Foundation, has named Dr. Timothy M. Miller as the recipient of the 2018 Sheila Essey Award for ALS Research. Dr. Miller received the award for his work to find effective therapies for ALS. The \$50,000 award is made possible through the generosity of the Essey Family Fund through The ALS Association Golden West Chapter, in memory of Sheila Essey, who battled ALS for 10 years and died from the disease in 2004.

Dr. Miller commented, “My group is very proud to receive the recognition of the distinguished Sheila Essey Award. This honor injects fresh energy into our continued day-to-day pursuit of new therapies for ALS. We intend to use the award to push forward the boundaries of knowledge about this disease by supporting some cutting-edge ideas that otherwise might not receive support in the early stages. This award will therefore serve as a springboard for this innovative work.”

The Miller Lab continues to pursue new targets for therapies, with particular interest in the molecules, called micro RNAs, that control how much of particular genes are expressed. Another focus of research involves determining the length of time certain building blocks of cells, called proteins, last in the body. This information will be used to guide future clinical studies and may provide new insights into the causes of ALS.

According to Dr. Miller, the explosion in genetics will continue to reveal an increasing number of clear targets for therapeutics. This expanded knowledge coupled with new tools to more sharply focus therapies such as antisense oligonucleotides, viral delivery and smart design of small molecules suggests an increasing number of therapeutics on the horizon for ALS.

Dr. Miller was honored at the American Academy of Neurology’s 70th Annual Meeting in Los Angeles, April 21-27.



*Ericka Simpson, MD, presents Sheila Essey Award to Timothy Miller, MD, PhD, and David Clayson Professor of Neurology at Washington University School of Medicine.*

## SOD1 ASO Trial Update

Many cases of ALS are sporadic; however roughly 10% of ALS has a genetic cause. These genetic forms of ALS are a rapidly growing area of research and hold promise for the development of effective therapies. Washington University is participating in Biogen’s Phase I trial of BIIB067, which is an antisense oligonucleotide (ASO) targeted at the SOD1 gene. ASOs are molecules delivered via lumbar puncture that target and bind to mRNA in order to prevent the production of specific disease-related proteins (in this case SOD1).

Washington University has been involved in the development of ASOs for ALS since Dr. Timothy Miller led the first in-human clinical trial of the SOD1 ASO from 2010 to 2011, demonstrating that this therapy is safe. This success led to the launch of Biogen’s larger Phase I/II trial currently underway at Washington University and other ALS centers around the world. Similar drugs have already reached FDA approval with other disorders such as Spinal Muscular Atrophy and are also in development for other ALS genes including C9Orf72.

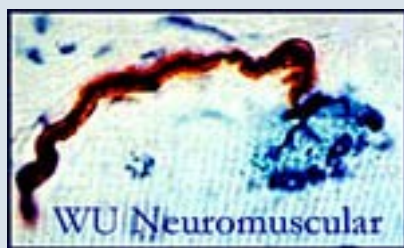
Results of Dr. Miller’s recent research to develop the ASO that is currently being used in the clinical trial were published in the August 2018 edition of the *Journal of Clinical Investigation*. While the subset of genetic ALS is relatively small, learning more about these cases will lead to a greater understanding and better treatments for all forms of ALS. Washington University and the Miller Lab are proud to continue to be at the forefront of these developments.

## Research Collaboration to Identify Tracer for TDP-43

Transactive response DNA binding protein 43 kDa (TDP-43) is a protein that commonly aggregates in neurons in patients with ALS as well as some forms of dementia. Currently, we can only determine whether patients harbor TDP-43 aggregates at the time of death when an autopsy is performed and brain tissue is examined under a microscope. TDP-43 aggregates are found in >95% of ALS and 25~50% of dementia post-mortem cases. The ability to detect TDP-43 aggregates during the course of disease would be immensely valuable for diagnosis, monitoring disease progression, and assessing the efficacy of therapeutics.

A team of scientific researchers has been assembled to develop a tracer for TDP-43 that binds to inclusions in real time and can be imaged non-invasively by positron emission tomography (PET), a standard clinical imaging technique. This multi-disciplinary team possesses wide-ranging expertise that will be necessary to tackle this ambitious endeavor including knowledge in ALS (Dr. Tim Miller, Washington University), PET tracer development (Dr. Vijay Sharma and Dr. Paul Kotzbauer, Washington University), TDP-43 biochemistry (Dr. Yuna Ayala, Saint Louis University), and TDP-43 pathology (Dr. Nigel Cairns, Washington University). This effort is supported by The ALS Association and ALS Finding a Cure.

The initial aim of this project involves identifying compounds that can tightly bind TDP-43 inclusions in biochemical and cellular assays as well as post-mortem tissue from ALS and/or FTD patients. The availability of post-mortem tissue for analysis of these tracers is important to continued progress and success of this effort. We appreciate the vital support of participants and families who donate tissue samples and enable ALS research, such as this study, to proceed. Several promising candidate tracers have already been identified. We aim to develop a TDP-43 PET tracer that can be advanced to clinical trials. The ultimate goal is to generate a TDP-43 PET tracer that will allow detection of TDP-43 burden in living patients and help inform physicians regarding the diagnosis and progression of ALS and dementia.



<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.

### Miller Lab Members Receive Recognition

The Miller Laboratory is proud to announce that two members have recently received special recognition from the Washington University research communities for their work in ALS research. In March, Dr. Mariah Hoyer received the James L. O'Leary Prize, awarded annually in recognition of the most original and important accomplishments in Neuroscience by researchers. In April, Alex Cammack received a research award from the Hope Center for Neurological Disorders for his research on C9ORF72-related ALS.

### How can you help The Miller Lab?

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:

Attn: Zach Silvers, Washington University, CB 1247  
7425 Forsyth Blvd.  
St. Louis, MO 63105



*Staff members from the Miller Lab teamed up at Forest Park on July 23rd to provide information and support the Walk to Defeat ALS®*