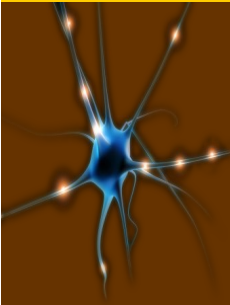


Summer,
2017



WASHINGTON UNIVERSITY DEPARTMENT OF NEUROLOGY

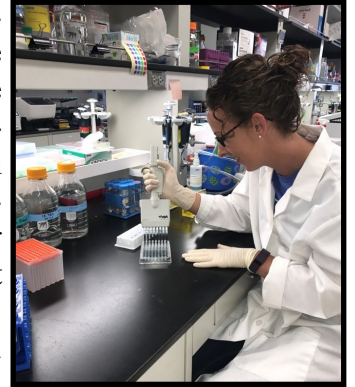
ALS Research Update

Antisense Oligonucleotides as a Potential Treatment for Human Neurodegenerative Diseases

Many neurodegenerative diseases, including ALS, are characterized by the accumulation of various toxic proteins within the brain or spinal cord. Antisense oligonucleotides (ASOs) are small DNA-like chemicals that can bind to and cause the destruction of toxic proteins, thereby reducing their accumulation and ultimately slowing disease progression. A Spring 2017 publication by Dr. Kathleen Schoch, a postdoctoral research scholar in the Miller Lab, explores the increased use of ASOs to treat neurodegenerative diseases.

Published in the highly regarded journal *Neuron*, Dr. Schoch's review article begins by highlighting the chemical modifications and pre-clinical animal studies that were necessary to enable the translation of ASOs from rodents to human patients. Since the first ASO clinical trial in 1993, ASOs have been pivotal in the treatment of spinal muscular atrophy, completing Phase III status and achieving FDA drug approval within the past year. Not too far behind are ASO therapeutics for Duchenne muscular dystrophy, for which the FDA has granted accelerated approval, and Huntington's disease, in which clinical trials are ongoing. Dr. Miller has been involved in ASOs for the treatment of ALS since the beginning and is the lead advisor for the Phase II clinical trial using ASOs for SOD1-associated ALS.

"Given their widespread application, advancements in design, and achievements in clinical applications, ASOs continue to garner enthusiasm for the treatment of many human diseases," Dr. Schoch writes. The research studies that ALS patients and families graciously consent to participate in at Washington University contribute to the advancement of therapies, including ASOs, for ALS. To view Dr. Schoch's publication and other articles from the Miller Lab, please visit: <https://millerlab.wustl.edu/research/publications/>



Kathleen Schoch, PhD, explores ASO strategies for neurodegenerative diseases in the Miller Lab.

GTAC Study Explores Interaction of Genes and Environment

Genomic Translation for ALS Care (GTAC) is a new study that aims to redefine our understanding of how genes and the environment interact to cause ALS. While researchers have known for decades that mutations in single genes play a clear role in one out of ten cases of ALS they have also long suspected that interactions between multiple genes play a role in a larger fraction of ALS. In these cases, one mutation is not harmful enough to cause symptoms on its own, but leads to ALS when combined with others.

Now, revolutions in technology and our understanding of genetics are allowing scientists to search for complex interactions among thousands of genes that may cause some people to develop disease while sparing others. Using these cutting edge techniques, GTAC aims to use DNA and blood from 1,500 individuals with ALS to improve our understanding of ALS and to define subtypes of ALS based on specific genetic patterns. Knowing how ALS patients differ from one another may allow us to understand and predict why some treatments work well for some patients but not others. The long term goal is to use genetic markers to determine the best individualized treatment strategy for each patient.

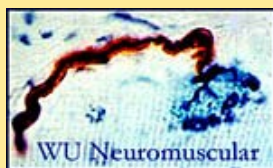


Timothy Miller, MD, PhD, discusses research study opportunities at Washington University during an ALS Expo coordinated by the Muscular Dystrophy Association in St. Louis.

A Collaborative New Research Platform for ALS Families

The Miller Lab in collaboration with Dr. Katie Nicholson of Massachusetts General Hospital has launched a new multicenter research study aimed at studying and helping families who have a history of inheriting ALS. People who are at genetic risk for developing the disease are often interested in participating in ALS research, but the majority of research studies currently involve only patients who are already symptomatic for ALS. Importantly, these gene carriers may also provide crucial information about the changes that the body undergoes prior to symptoms, which can help researchers understand how to target and block those negative changes for potential therapeutic strategies.

Called the Dominant Inherited ALS Network, or “DIALS” for short, this research platform will evaluate people at high risk for ALS with the goal of discovering genes that prevent ALS, identify early diagnostic signs before symptoms occur, and ultimately delay or prevent the onset of ALS. Families will have the opportunity to undergo testing for their exact genetic cause of ALS and will be studied long-term in order to detect biomarkers of disease initiation. By involving people who have a desire to participate in research and who can provide highly valuable information to researchers, DIALS has the potential to become a collaborative experience that enriches the knowledge of both researchers, patients and family members.



<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

Rainwater Tau Consortium

Ionis Pharmaceuticals

Biogen Idec MA Inc.

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. 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

***The Walk to Defeat ALS[®]
is just around the corner!***

Date: Saturday, June 24th

***Location: Forest Park Visitor's Center
parking lot***

***Check in: 8:30am; Walk starts at 10am
The Miller Lab group will be there! Stop
by the Washington University table!***



***Staff from the Washington University School of Medicine
Department of Neurology teamed up at Forest Park on
April 2nd to support the annual MDA Muscle Walk.***