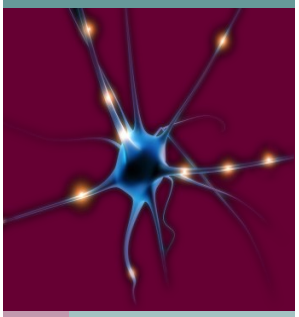
Summer, 2016



WASHINGTON UNIVERSITY DEPARTMENT OF NEUROLOGY

ALS Research Update

Answer ALS seeks to resolve ALS puzzle

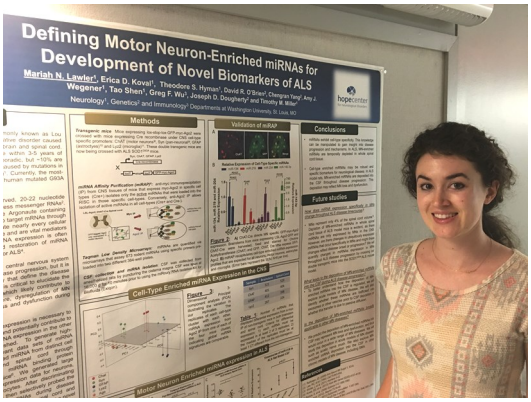
Timothy Miller, MD, PhD, leads the Answer ALS efforts at Washington University.

Washington University's Neuromuscular Division is proud to be a leading site for Answer ALS, a groundbreaking study investigating the causes of ALS. Funded by the ALS Finding a Cure Foundation and coordinated by our collaborators at Massachusetts General Hospital and Johns Hopkins University, this new study represents not only one of the largest scientific collaborations in the history of ALS research, but also possibly the most in depth study of the mechanisms underlying this disease. The goal of Answer ALS is simply to answer "why?" Why does ALS strike certain people, while leaving the vast majority of the population unaffected? What is different about the people who develop this condition?

Answer ALS aims to resolve these puzzles by applying new advancements in the fields of stem cell research, genomics, proteomics, and metabolomics to investigate what makes those with ALS susceptible to this disease. These methods in tandem with the participation of over a dozen large medical centers and hundreds of patients, will produce the most in depth set of data ever collected describing ALS. These data will give researchers at Washington University and around the world the clearest picture yet of how ALS develops and progresses. With luck, and hard work from patients and scientists alike, these new insights will allow doctors to identify ALS early, treat it effectively, and prevent it in the future.

The Washington University research team is actively recruiting participants for Answer ALS. Enrolling in the study requires approximately two hours, which includes questionnaires, tests for muscle strength and breathing, and a blood draw. Patients can also choose to undergo an optional lumbar puncture to donate cerebrospinal fluid to the study.

Biomarkers Study Facilitates MicroRNA research



Mariah Lawler is a PhD Candidate working in Dr. Miller's lab. She is studying the role of microRNAs in various neuromuscular diseases.

Samples donated to the Biomarkers Study by ALS patients and control participants have facilitated many different important areas of ALS research. In particular, a research project in the Miller lab has used these samples to define a potential biomarker of ALS disease progression, a molecule that can be measured to inform physicians about a patient's current disease state.

The Miller lab has been studying a group of potential biomarkers called microRNAs, which are small molecules located throughout the body that can turn various processes on or off inside a cell. By analyzing which microRNAs were located in cells of the body that were affected by ALS neurodegeneration versus cells that were not affected by disease, they were able to pinpoint one microRNA that was frequently found at high levels in cells affected by ALS. Therefore, this microRNA may be a good representation of exactly how much neurodegeneration an ALS patient is experiencing.

While these experiments using human samples and rodent models of ALS will need to be further tested to validate the findings, the Miller lab may have discovered a useful biomarker of ALS. We thank all patients and other participants for their continued support in contributing blood and cerebral spinal fluid to the Biomarkers Study.

Collaboration with Dr. Robert Baloh

Changes in the C9orf72 gene account for about 30% of familial ALS and 5-10% of sporadic ALS. The "orf" part of the gene name stands for "open reading frame," which in genetic terms means we know that this is an important part of the genome, but the function of the gene is unclear.

One way to determine the importance of an unknown gene region is to delete that region in mice and determine how this affects the mouse model. Our collaborators at Cedars Sinai Medical Center in Los Angeles, led by Dr. Robert Baloh, took this approach. Somewhat surprisingly, they found that loss of this gene region led to changes in cells of the immune system, thus refocusing ALS researchers on what these immune system related cells might be doing in ALS. Dr. Baloh and colleagues recognized the importance of linking these new findings to humans with the disease and subsequently used spinal cord samples donated from ALS patients at Washington University in St. Louis. Strikingly, these human samples showed some changes similar to the mouse models and thus helped demonstrate the relevance of the mouse studies to humans.

Collaborative studies like these that benefit ALS research overall are made possible by the generous participation of patients in the Washington University Neuromuscular Clinic.

More information about this study can be found in the following research article: O'Rourke JG, Boqdanik L, Yanez D, et al. C9orf72 is required for proper macrophage and microglial function in mice. Science. 2016 Mar;351(6279):1324-1329. PMID: 26989253. http://www.ncbi.nlm.nih.gov/pubmed/26989253

WU Neuromuscular

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.

Staff from the Washington University School of Medicine Department of Neurology teamed up at Forest Park on April 3rd to support the MDA Muscle Walk.

How can you help The Miller Lab?

Charitable donations support ALS research

For contributions to the Washington University ALS program, please contact Zach Silvers, 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
425 Forsyth Blvd., Suite 2100, St. Louis, MO 63105

Tissue donation is a gift to future generations

The causes of most neuromuscular diseases are poorly understood and treatments are rare. It is our hope that patient autopsies and tissue donations will provide researchers with the tools needed to:

- Understand the cause and course of the disease
- Design better and more accurate diagnostic tests
- Promote the development of treatments

To obtain additional information, please call 314-362-6159 or email: neuroclinicalstudies@neuro.wustl.edu