

Brandeis scientists work to understand the disease behind the ‘Ice Bucket Challenge’
By Leah Burrows

The ALS Ice Bucket Challenge is simple: Donate \$100 to an ALS charity or dump a bucket of ice water on your head and donate \$10. Millions of people around the world have taken the challenge, including Justin Timberlake, Bill Gates and Olympian Tim Morehouse '00.

The challenge is simple but finding a cure for ALS is not.

Amyotrophic lateral sclerosis, more commonly known as Lou Gehrig’s disease, is a neurodegenerative disease marked by the rapid, progressive death of motor neurons that control muscle movements. It currently afflicts about 30,000 Americans but scientists are still trying to understand what causes the disease.

At Brandeis University, professors Suzanne Paradis and Avi Rodal are working to unravel the molecular mechanics of ALS. BrandeisNow spoke with Paradis and Rodal about the real challenges in finding a cure for this deadly disease.

What makes ALS so challenging to treat?

The major challenge in finding treatments for ALS is identifying the cellular and molecular basis of the disease. The majority of ALS patients have what is called sporadic ALS, meaning there is no family history of the disease. We’re not sure yet what leads to ALS in these sporadic cases, whether it’s environmental factors, genetic factors, or some combination of both.

In order to treat ALS, we have to understand what the cells of these patients have in common. If we can understand what leads to the neurodegeneration, it might lead us to drug targets that can help slow the progression of the disease and reduce neuronal death.

The fast pace of neurodegeneration makes ALS a devastating disease. Unfortunately, it is likely that much of the damage has already occurred by the time a diagnosis is made, so another challenge is early detection before damage might be irreversible.

What strides have researchers made in recent years in understanding this disease?

In recent years, the research community has made enormous advances in understanding the genetic basis of ALS. For example, a 2011 study identified mutations in a gene called C9orf72 as the most widespread cause of ALS. Similarly, aggregates of an RNA binding protein called TDP43 have been found in the majority of sporadic cases of ALS. Identification of these and other targets has opened new avenues of inquiry into the cellular and genetic basis of ALS and offered potential targets for new drugs.

How is your research trying to understand the disease?

Our muscles secrete proteins called growth factors, which help motor neurons — the neurons that control muscle movement — develop. Neurons must carefully package and sort these growth **factors** in order for them to function properly. We are working to understand how **these**

sorting and packaging processes may go wrong in ALS. We are focusing on how **growth factors are transported within the neuron and how mutations causing ALS alter this process in fruit flies.**

At the same time, we are working to develop a system to study these **growth factors** in mammalian neurons, to test if there are defects comparable to those we see in the flies. We have found that growth of these neurons is severely affected when they are modified to express TDP43. We are now testing if these defects are related to problems with specific **growth factors** as well as whether other genes implicated in ALS produce similar defects in mammalian neurons.

By understanding how **growth and survival factors** are being diverted from their normal itinerary in diseased neurons, we hope we can develop new therapies to return these signals to the appropriate location.

How has the ALS research community reacted to the ALS Ice Bucket Challenge?

Our work is supported by the [Blazeman Foundation for ALS](#), an organization that has been working for years to raise awareness of ALS and funding towards a cure. They are blown away by how powerful the ice bucket challenge has been in both educating the public and raising funds for research. Finding a cure may not be as easy as dumping an ice bucket on your head, but support for research is the first essential step towards a cure.