

Ice Bucket Challenge Funds Major ALS Research Finding

By Kasra Zarei

kasra-zarei@uiowa.edu

The ice bucket challenge funded a major research finding related to amyotrophic lateral sclerosis (ALS), recently published in the journal *Nature Genetics*. University of Iowa physicians and researchers share their reactions.

Millions of people participated nationally in the ice bucket challenge two years ago, raising an estimated \$115 in the process.

While the social media phenomenon was criticized for being a fad where most participants did not know what ALS is, two years later the effort had funded a major finding in ALS research.

A recently published study conducted by over 80 researchers spanning 11 countries identified an association of the NEK1 gene with ALS. In the study, variants of NEK1 gene, as well as several other genes characterized in previous studies, are associated with increased susceptibility to ALS.

The finding further links the pathology of ALS to pathways involved in DNA damage response and maintenance of neuronal processes.

The work has excited researchers in the field including Andrew Pieper, UI professor of psychiatry and neurology, whose work focuses on studying neuroprotective compounds with applications to ALS.

“The reported association is an exciting finding, both scientifically and for the fact that it was enabled by a massive socially-driven fund raising effort in a time when traditional sources of funding for scientific research have become more difficult to secure,” Pieper said.

Besides providing new, important insights concerning the genetic basis of ALS, the discovery funded by the ice bucket challenge provides another potential target for therapy development for patients with ALS

According to Weam Shahin, UI postdoctoral scholar, among the key challenges in the treatment of ALS is late identification of patients.

“By the time paralysis occurs and diagnosis is made, lower motor neurons are already dead or irreversibly injured. This limits the potential benefits of therapies and explains the multiple failed trials currently observed,” Shahin said.

With the advances in DNA sequencing technologies, identifying these genetic variants could aid in the early diagnosis of ALS or determine whether individuals are at increased risk of developing this disease.

“The lack of early diagnostic tools and the diverse etiology of ALS make it challenging to develop an effective treatment,” Shahin said. “Dissecting the pathogenesis of ALS following the diverse contributors to the disease will identify the common affected pathways and novel targets for more effective therapies for ALS.”

To validate the association of NEK1 genetic variants with ALS susceptibility, prospective cohort studies are required as the next step to ensure that the proposed markers accurately identify future ALS patients.

“Starting with young subjects carrying these genetic variants and following them to establish the causation of the proposed genetic differences on the natural history of the disease is imperative,” Shahin said. “Simultaneously, studying animal models carrying these human genetic variants will elucidate the role of these genetic variants in ALS development and prognosis.

Genetic variants involved in ALS are of particular interest to many researchers including Shahin, who is working to create personalized medical approaches for ALS with John Engelhardt, UI professor of internal medicine and anatomy and cell biology.

“Individuals carrying certain known genetic variants are more susceptible to ALS development and more responsive to certain types of treatment,” Shahin said.

A personalized approach to treating ALS is crucial in selecting the most suitable treatment for the right patients early in the course of the disease and thus improving the efficacy of treatment.

What is not known to most people is that ALS is different for every person, and personalized treatment and care approaches are needed to provide the maximum benefit and comfort to patients.

Andrea Swenson, UI clinical assistant professor of neurology, works in the ALS clinic and emphasizes the personalized approaches needed to also care for patients.

“Our multidisciplinary ALS clinic at the University of Iowa offers an individualized approach - our goal is to help our patients live with ALS,” Swenson said. “Our team of physicians, nurses, and therapists guide patients through the stages of the disease, provide resources and support for patients and their families, and offer hope through clinical trials and research.”