MedicalXpress

ALS study reveals a unique population

January 19 2021

Malta, a sovereign microstate in the middle of the Mediterranean Sea, has no shortage of sunny beaches, honey-bricked villages and rugged countryside. Beyond its Mediterranean charm, Malta is home to a geographically and culturally isolated population whose unique genetic makeup, makes this island nation a goldmine for genetics research.

Four years ago, the University of Malta set up a national ALS Registry and Biobank to identify patients with amyotrophic lateral sclerosis (ALS) and collect data on their residence, occupation, lifestyle and environmental exposures. Blood samples donated by participants will remain stored in high-tech storage facilities at the University over many years.

ALS is a progressive neurological disease that destroys the nerves that interact with the body's muscles. The disease typically leads to complete paralysis of the body, robbing patients of their ability to walk, speak, eat and breathe. There is no cure for ALS, and eventually, the disease is fatal.

Malta's ALS Biobank is providing scientists with an invaluable resource for understanding the causes of ALS. In the first landmark study, researchers have retrieved and scrutinized the DNA from blood samples to discover flaws in genes linked to ALS.

"The DNA results caught us by surprise. The most frequently mutated ALS genes were flawless in Maltese patients," said the study's lead researcher Dr. Ruben J. Cauchi, Ph.D., a senior lecturer at the

University's School of Medicine and lead investigator at the University's Centre for Molecular Medicine and Biobanking.

Collaborating with scientists at the University Medical Centre (UMC) Utrecht in The Netherlands, University of Malta researchers found that ALS patients in Malta did not have flaws in the C9orf72, SOD1, TARDBP and FUS genes, which are known to contribute to a major number of ALS cases worldwide.

The study nonetheless revealed that compared to other European populations, a higher percentage of Maltese patients with no prior family history of ALS have harmful flaws in their DNA. Intriguingly, these occur in genes that are rarely damaged in Europeans with ALS.

"Our results underscore the unique genetics of the Maltese population, shaped by centuries of relative isolation. We also established that genetic factors play a significant role in causing ALS in Malta," added Dr. Cauchi.

Right now, the research team is on the hunt for what triggers ALS in more than half of the study subjects that had no flaws in known ALS genes. Thanks to the participation of patients and healthy volunteers, Malta's ALS Biobank is rapidly growing into a precious treasure trove of data that is expected to unveil more fascinating insights on the causes of ALS in the years to come.

More information: Rebecca Borg et al, Genetic analysis of ALS cases in the isolated island population of Malta, *European Journal of Human Genetics* (2021). DOI: 10.1038/s41431-020-00767-9

Provided by University of Malta