03/2019

Amyotrophic lateral sclerosis (Nicolas, 2019)

Aude Nicolas, et al.
Neuron

Muscles | Spine | Brain

STUDY SUMMARY

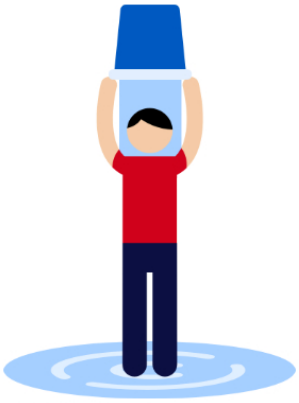
Discovery of genetic variants in the KIF5A gene that are associated with amyotrophic lateral sclerosis (ALS).

YOUR RESULT

Below average genetic predisposition to **amyotrophic lateral sclerosis**

STUDY DESCRIPTION

Amyotrophic lateral sclerosis, or ALS, is a progressive degeneration of nerve cells that control muscle movements which results in worsening weakness. ALS patients lose the ability to walk, use their hands, speak, swallow, and eventually breathe. This study analyzed the genomes of over 20,000 ALS patients of European ancestry and discovered a novel ALS-associated gene. The KIF5A gene encodes a protein that functions as a motor that helps transport cargo within cells. In nerve cells, motor proteins like KIF5A play an important role in transport along nerve fibers. Nerve cells that control movements have particularly long nerve fibers that might be particularly susceptible to disruption of cellular transport.



The Ice Bucket Challenge that promotes awareness of ALS went viral in the summer of 2014.

DID YOU KNOW?

Smoking and exposure to environmental toxins (e.g. lead) might trigger ALS. Early signs of ALS include chronic muscle cramps, twitches, weakness in the hands and feet, and a loss of balance.

YOUR DETAILED RESULTS

To calculate your genetic predisposition to amyotrophic lateral sclerosis we summed up the effects of genetic variants that were linked to amyotrophic lateral sclerosis in the study that this report is based on. These variants can be found in the table below. The variants highlighted in green have **positive effect sizes** and increase your genetic predisposition to amyotrophic lateral sclerosis. The variants highlighted in blue have **negative effects sizes** and decrease your genetic predisposition to amyotrophic lateral sclerosis. Variants that are not highlighted are not found in your genome and do not affect your genetic predisposition to amyotrophic lateral sclerosis. By adding up the effect sizes of the highlighted variants **we calculated your polygenic score for amyotrophic lateral sclerosis to be -0.63**. To determine whether your score is high or low, we compared it to the scores of 5,000 other Nebula Genomics users. We found that your polygenic score for amyotrophic lateral sclerosis is in the **31st percentile**. This means that it is higher than the polygenic scores 31% of people. We consider this to be a **below average genetic predisposition to amyotrophic lateral sclerosis**. However, please note that genetic predispositions do not account for important non-genetic factors like lifestyle. Furthermore, the genetics of most traits has not been fully understood yet and many associations between traits and genetic variants remain unknown. For additional explanations, click on the column titles in the table below and visit our Nebula Library tutorial.

VARIANT	YOUR GENOTYPE	COMMENTS	EFFECT SIZE	VARIANT FREQUENCY	SIGNIFICANCE
rs3849943_T	T / T	-	-0.17 (↓)	76%	3.80×10^{-30}
rs12973192_C	C / G	-	-0.12 (↓)	68%	3.90×10^{-16}
rs75087725_A	NA	-	0.51 (-)	1%	1.80×10^{-14}
rs142321490_C NEW	NA	In KIF5A gene	0.31 (-)	2%	6.10×10^{-10}
rs113247976_T NEW	NA	In KIF5A gene	0.32 (-)	2%	6.40×10^{-10}
rs116900480_T NEW	NA	In KIF5A gene	0.31 (-)	2%	6.60×10^{-10}
rs74654358_A	NA	-	0.20 (-)	4%	4.70×10^{-9}
rs118082508_T NEW	NA	In KIF5A gene	0.31 (-)	1%	2.00×10^{-8}
rs117027576_G NEW	NA	In KIF5A gene	0.31 (-)	1%	2.30×10^{-8}
rs10463311_T	T / T	-	-0.08 (↓)	75%	4.00×10^{-8}

N/A indicates variants that could not be imputed using the 1000 genomes project datasets and variants that have a frequency of < 5%. Your genome was sequenced at 30x/100x coverage and is not imputed. However, to calculate percentiles, we need to compare your data with other users imputed data. To make the data comparable, we need to exclude some of the variants from your data.