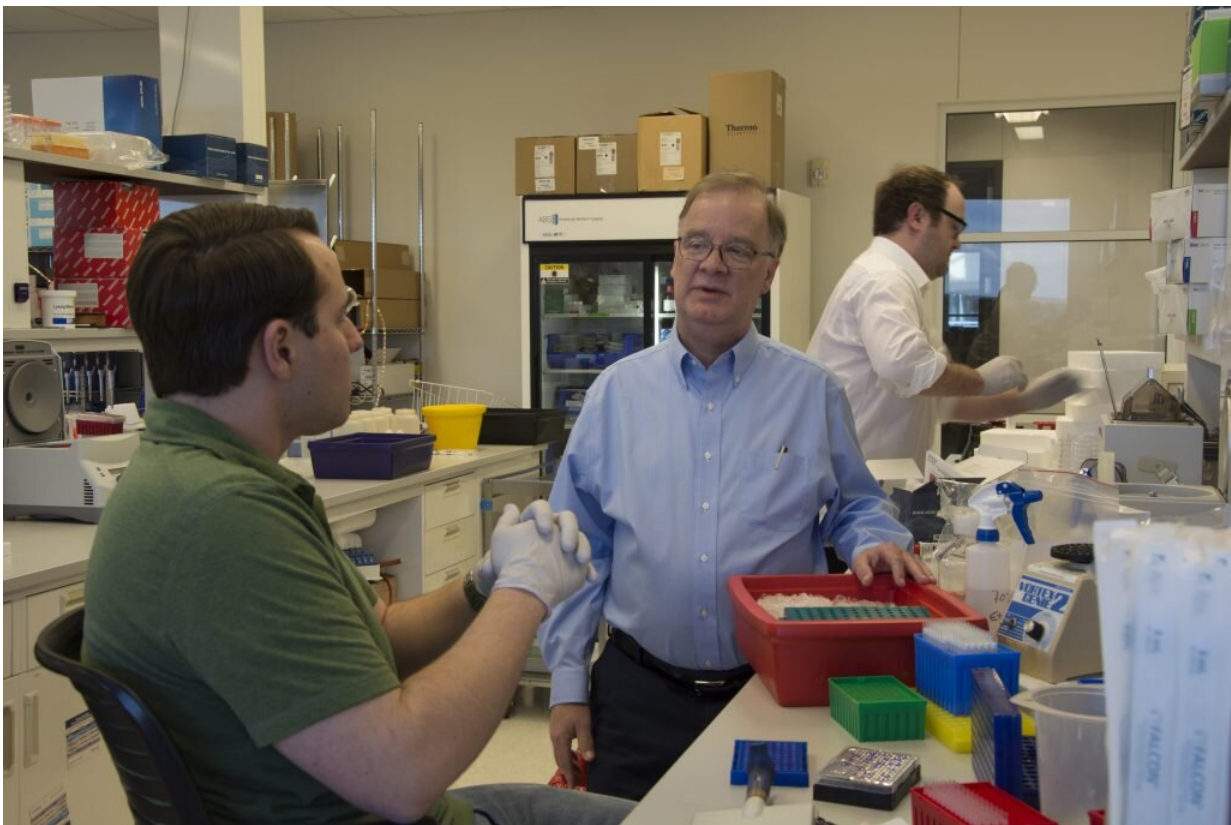


Scientists uncover a gene that doubles the risk of developing several neurodegenerative diseases

April 27 2020



Richard M. Myers, PhD, and Nicholas Cochran, PhD, in the Myers Lab at HudsonAlpha Institute for Biotechnology. Credit: HudsonAlpha Institute for Biotechnology

Scientists at the HudsonAlpha Institute for Biotechnology, the University of California, San Francisco (UCSF), and the University of Alabama at Birmingham (UAB), have identified a new risk factor for multiple neurodegenerative diseases.

"Finding evidence for a risk factor that contributes to multiple [neurodegenerative diseases](#) is exciting," said Richard M. Myers, Ph.D., HudsonAlpha president and science director. "We already know that these diseases share some pathologies. This work shows that the underlying causes of those pathologies may also be shared."

In the study, which was published April 23 in the *American Journal of Human Genetics*, researchers sequenced and analyzed whole genomes of more than 1,100 people. They found that rare variation in the gene TET2 nearly doubled the risk of developing diseases like Alzheimer [disease](#) (AD), [amyotrophic lateral sclerosis](#) (ALS), and [frontotemporal dementia](#) (FTD).

"The project wouldn't have been possible without extensive collaboration between institutions," said first author Nicholas Cochran, Ph.D., a senior scientist in the Myers Lab. "You end up being able to find things that you can't find working alone."

Jennifer Yokoyama, Ph.D., an assistant professor of neurology at UCSF, worked with Cochran on technical details and also was the point person for sample collection. The majority of the samples used for the project were collected over decades at the UCSF Memory and Aging Center and then sequenced and analyzed at HudsonAlpha.

Once the research team had the sequence results, they analyzed the genomes of 493 people with either AD, ALS, or FTD and 671 healthy people. Many of the patients had early-onset versions of neurodegenerative disease, which suggests that it is more likely that there

would be a genetic component of their illness. During genome analysis, the researchers looked at both coding and non-coding regions of the genome for DNA sequence variants, a strategy that allowed them to be more confident that any possible genes they pulled out were the real deal.

"We didn't go in with any suspicions about what we might [get], so we're excited that we did find a new genetic association here," Cochran said. TET2 is especially exciting because it encodes a protein that catalyzes DNA demethylation. Previous work has shown that changes in DNA methylation happen during aging, so the authors hypothesize that mutations in the gene could lead to a faulty TET2 protein that disrupts how the brain ages and contributes to the development of neurodegenerative diseases.

"Sometimes we get a hit, and it's hard to understand what it might be doing, but TET2 already has established roles in the brain. So this finding really made sense," Cochran explained.

After the team identified TET2, they looked at previously generated [genetic data](#) from more than 32,000 healthy people and people with neurodegenerative diseases. This data confirmed that variants in TET2, in both protein-coding and non-coding regions, were more likely to be present in the genomes of people with AD, ALS, or FTD than in people without these diseases. Next steps will focus on how changes in TET2 levels or function could contribute to aging and neurodegenerative disease.

More information: J. Nicholas Cochran et al. Non-Coding and Loss-of-Function Coding Variants in TET2 are Associated with Multiple Neurodegenerative Diseases, *The American Journal of Human Genetics* (2020). [DOI: 10.1016/j.ajhg.2020.03.010](https://doi.org/10.1016/j.ajhg.2020.03.010)

Provided by HudsonAlpha Institute for Biotechnology

Citation: Scientists uncover a gene that doubles the risk of developing several neurodegenerative diseases (2020, April 27) retrieved 24 April 2024 from <https://medicalxpress.com/news/2020-04-scientists-uncover-gene-neurodegenerative-diseases.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.