TOOLBOX

New method taps family trees for clues about conditions

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Asking participants in genetic databases about their family's medical history can help researchers uncover genetic variants tied to uncommon conditions such as autism[1].

The standard approach for unearthing genetic variants linked to a particular condition is a genome-wide association study (GWAS). For this type of study, scientists often must recruit tens of thousands of people with a condition to uncover statistically significant connections.

Amassing these numbers is much easier for common conditions, such as heart disease, than it is for ones such as autism.

The new approach, described 16 January in *Nature Genetics*, is called genome-wide association study by proxy (GWAX). It allows researchers to cast a wider net for variants by asking people in the general population what conditions their immediate relatives have. Because people share 50 percent of their DNA with each of their parents, siblings and children, the DNA of the participants holds clues to the conditions of these relatives.

A computer program statistically analyzes sequencing data and medical histories, and gauges the probability that any genetic variant that pops up in the analysis is associated with a condition.

Family matters:

Researchers tested the approach using data from the **UK Biobank**, a repository of genomic and medical information from about 500,000 people aged 40 to 69. Participants provided saliva samples for sequencing. They also completed questionnaires about 12 health conditions in their first-degree relatives. In the new study, the researchers analyzed records from about 116,000 of the 500,000 biobank participants.

One of these conditions is Alzheimer's disease. Only 55 of the 500,000 individuals in the biobank have Alzheimer's disease, but more than 60,000 have a parent with the condition. Using GWAX, the researchers uncovered four new variants associated with Alzheimer's disease; two of these affect genes involved in the immune response.

"We're able to uncover what we think is pretty interesting and exciting biology by applying this approach," says lead researcher **Joe Pickrell**, assistant investigator at the New York Genome Center.

Pickrell and his team also uncovered eight new variants associated with heart disease and five associated with type 2 diabetes.

The UK Biobank's questionnaire did not include autism, but future questionnaires could. GWAX could use similar databases to help researchers find variants relevant to autism.

REFERENCES:

1. Liu J.Z. *et al. Nat. Genet*. **49**, 325-331 (2017) **PubMed**