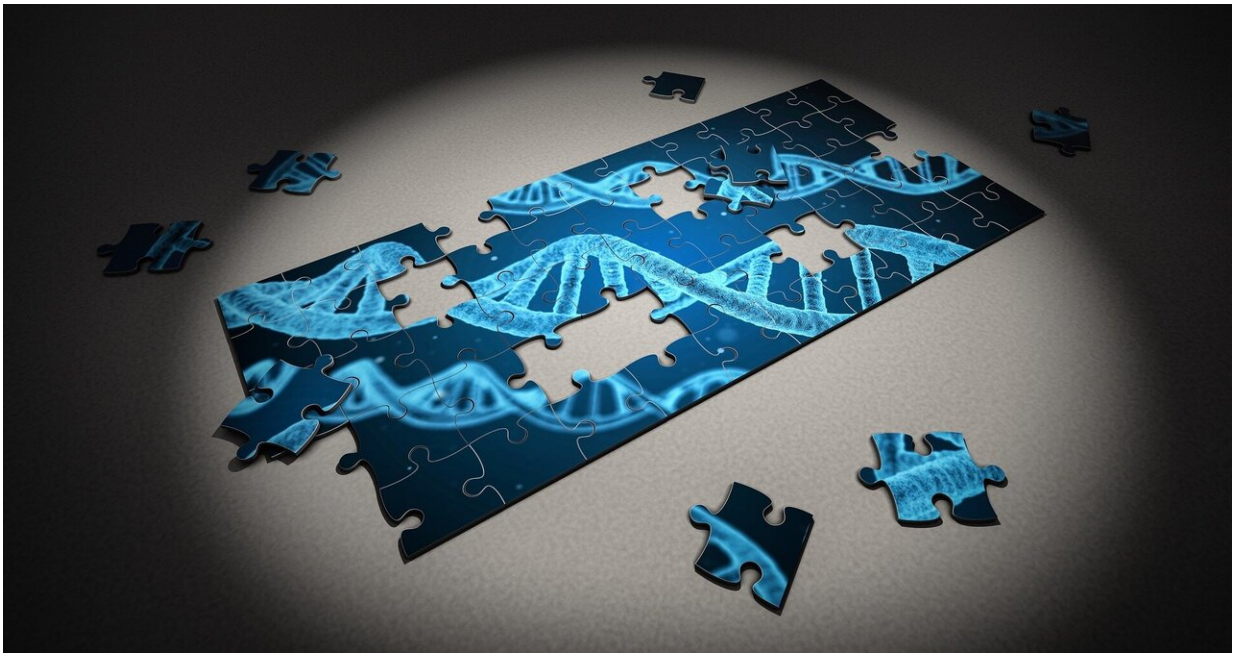
Unraveling the genetic puzzle of Alzheimer's disease

January 18 2024, by Darcy Millett



Credit: CC0 Public Domain

As Australia's population ages, we're hearing a growing number of stories about complex diseases with cognitive and behavioral effects.

Cognitive changes can impact memory, attention, and problem-solving. Meanwhile, behavioral effects involve alterations in how individuals act or respond to their environment. These kinds of symptoms can be the

result of neurodegenerative diseases, such as dementia. The rate of neurodegenerative diseases is expected to double over the next 40 years. So, chances are someone you know will be affected by dementia's most common form, Alzheimer's disease.

Complex diseases are, well, complex. Understanding how they develop, their signs, and how they can be managed is tricky. One aspect of complex diseases that can be especially difficult to research is heritability, or the way genes are passed along in a family.

Let's go back to the age-old question: Do our physical traits depend on our genetics or our environment? The answer is both.

Say, you have a close relative who has been diagnosed with Alzheimer's disease. You wonder whether you'll also develop it because it's "in your genes." As expected, the answer to this is not simple.

Everyone has observable traits or characteristics they are born with. These are called phenotypes. A good example is brown eyes. Having brown eyes is an observable expression of a certain genetic makeup.

Disease states have phenotypes as well. Disease phenotypes are the characteristics we can see when a person has a disease. For example, someone with Alzheimer's disease may present with memory loss.

Many characteristics depend on a mixture of our genetics and our environment. Figuring out how much a trait is influenced by either factor is necessary to manage and treat diseases.

Getting to the bottom of Alzheimer's heritability

The heritability of Alzheimer's has been estimated as high as 80%. You might look at this number and wonder, "Does this mean that I have an

80% chance of getting Alzheimer's if one of my parents has it?" Not exactly.

Heritability is a measure of how much the variation of a trait within a population is caused by a variation in genes. It is usually shown as a percentage value. This means that we can only apply a heritability value to a group of people—not an individual.

The exception is a form of Alzheimer's disease called familial Alzheimer's, where symptoms usually develop early on in a person's life. The chances of passing it on to their offspring is 50%.

The missing pieces in the genetic disease puzzle

This is where '"missing heritability" comes in. It's a big issue encountered in Alzheimer's disease research.

Missing heritability refers to when scientists know that a disease is heritable but are unable to find the underlying genetic cause.

For simple diseases, scientists can understand their heritability by finding genetic variants. Variants are different versions of the same gene which cause different phenotypes. However, with a complex disease like Alzheimer's, individual variants are not the sole cause of the disease. This makes solving the puzzle much more complicated.

Scientists now know that Alzheimer's is caused not only by gene variants, but also by the relationships between different genes.

We call these relationships gene interactions. Gene interactions can occur between the roughly 20,000 genes, meaning there are endless possibilities to how they can influence disease phenotypes.

Finding these interactions gives scientists the opportunity to highlight variants that can act as "modulators" in Alzheimer's disease. Modulators can either reduce or increase the chance of someone developing a disease, so identifying them is crucial to understanding Alzheimer's.

Traditional approaches to studying genetics are not powerful enough to find all these gene interactions. If scientists don't know what to look for, there is no way to find it. And doctors can't catch it until it's too late.

This is why curing and treating Alzheimer's is a challenge.

AI and machine learning for early genetic disease detection

Until recently, scientists have lacked tools powerful enough to capture the impacts of gene interactions. With the development of artificial intelligence and machine learning approaches such as our VariantSpark tool, we are beginning to see the full extent of how relationships between genes can help us understand disease.

The key to Alzheimer's research is adding the pieces of this missing heritability to the puzzle. This allows scientists to understand the causes and warning signs of the disease. It could allow at risk people to be identified sooner and enable early intervention strategies—both of which are vital to improving outcomes for patients.

Each piece of missing heritability we uncover brings us closer to more effective treatments and early intervention strategies. This progress is not just about solving scientific puzzles—it's about changing lives, offering hope, and building a future where diseases like Alzheimer's can be effectively managed.

Provided by CSIRO