Research project by
Dr Luke Gray Whiley

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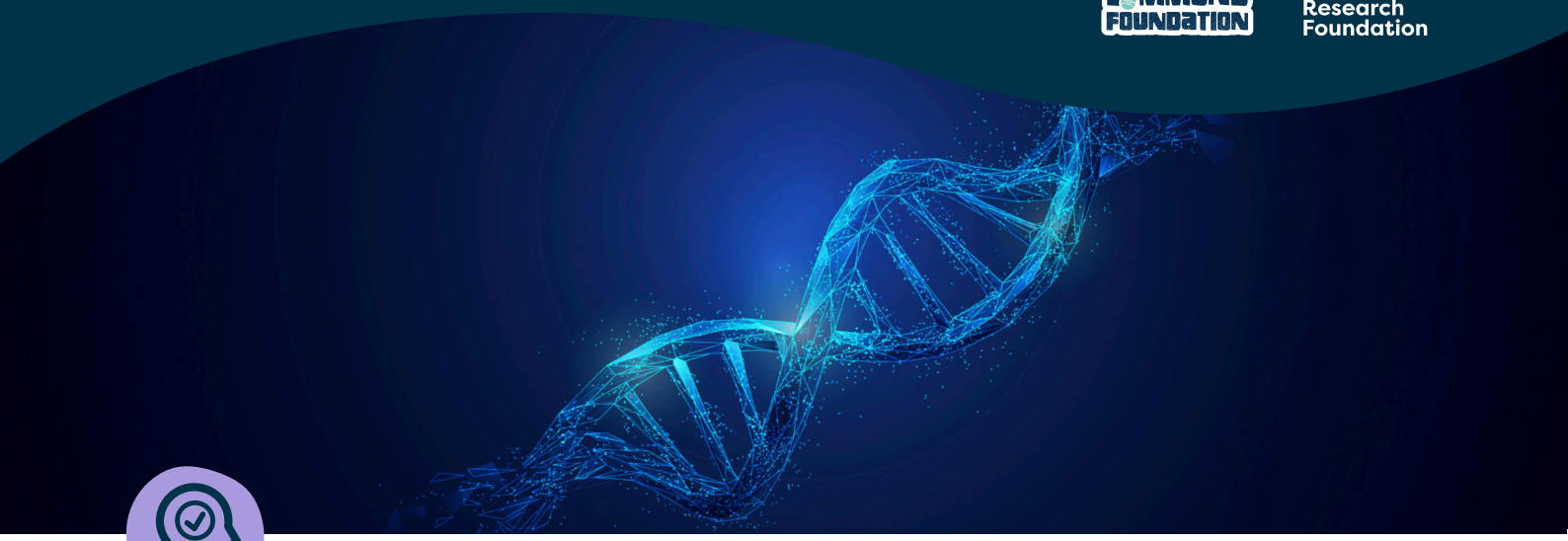

Understand

Solving gene variation mystery may uncover causes of Alzheimer's disease

What is the focus of the research?

Generating critical new knowledge of a specific gene variation that causes Alzheimer's disease.

Why is this important?

Alzheimer's disease is the most common type of dementia, but scientists still don't know exactly why it occurs. While specific variations in a person's genetics are known to increase the risk of developing Alzheimer's disease, how these genes are connected to its development remains a mystery.

This lack of knowledge is especially critical in genes common in all of us, such as ABCA7. ABCA7 helps to make a protein that moves cholesterol into and out of cells, a process that's important for cell heath.

However, one in six people carry a variation in ABAC7 that increases their risk of Alzheimer's disease by 20 per cent. Unfortunately, scientists don't know why. Before they can identify the factors that link ABCA7 to causes of Alzheimer's disease, they need to understand the role altered ABCA7 plays in the everyday function of a person's biology.

In this project, Dr Whiley aims to do exactly that. His project will generate critical new knowledge of the interaction between altered ABCA7 and human biological function.

This knowledge will lay the groundwork for understanding the biochemical factors that contribute to a person's risk of ABCA7-associated Alzheimer's disease before it develops. This will uncover opportunities for researchers to develop medical interventions that may prevent or delay Alzheimer's disease in these people.

How will it happen?

Stage 1: measure the chemical composition of blood samples collected from a large-scale healthy ageing study. Compare the chemical signature of people carrying the ABCA7 variant with those who don't, to reveal biological differences caused by the gene variant.

Stage 2: perform specialised statistical analysis of the chemical signatures to understand how they may change through ageing. Analysis will also reveal if the signatures are amplified by additional disease risk factors, including sex, BMI, diabetes and high blood pressure.

Stage 3: using human cells grown in a lab, study the effects that removing ABAC7 has on cell metabolism. Measure cells' chemical composition to understand how ABCA7 affects their function and development, and how specific biochemical pathways are influenced by the gene.

What will it mean for dementia research?

- New understanding of ABAC7's role in human biology.
- Potential insights into how ABCA7 increases Alzheimer's disease risk.
- New avenues to develop treatments that target ABCA7.

Who's undertaking the research?

Dr Luke Gray Whiley, Murdoch University

Dr Gray Whiley is a senior lecturer in phenomics, healthy ageing and dementia at the Health Futures Institute, Murdoch University. After completing his PhD at Kings College London, he held post-doctoral roles at the UK Dementia Research Institute and Imperial College London.

In 2021, Dr Gray Whiley was featured on the American Chemistry Society's rising star in metabolomics and proteomics (40 under 40) list. He actively works to communicate research to the public and is currently project officer for Perth's annual Pint of Science Festival. He has also appeared on ABC Perth Radio and national podcast series *Naked Science*, along with social media campaigns for various dementia charities.

The title of Dr Gray Whiley's project is *Advancing the understanding of genetic risk in sporadic Alzheimer's disease by elucidating the metabolic consequences of ABCA7 polymorphisms.*

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