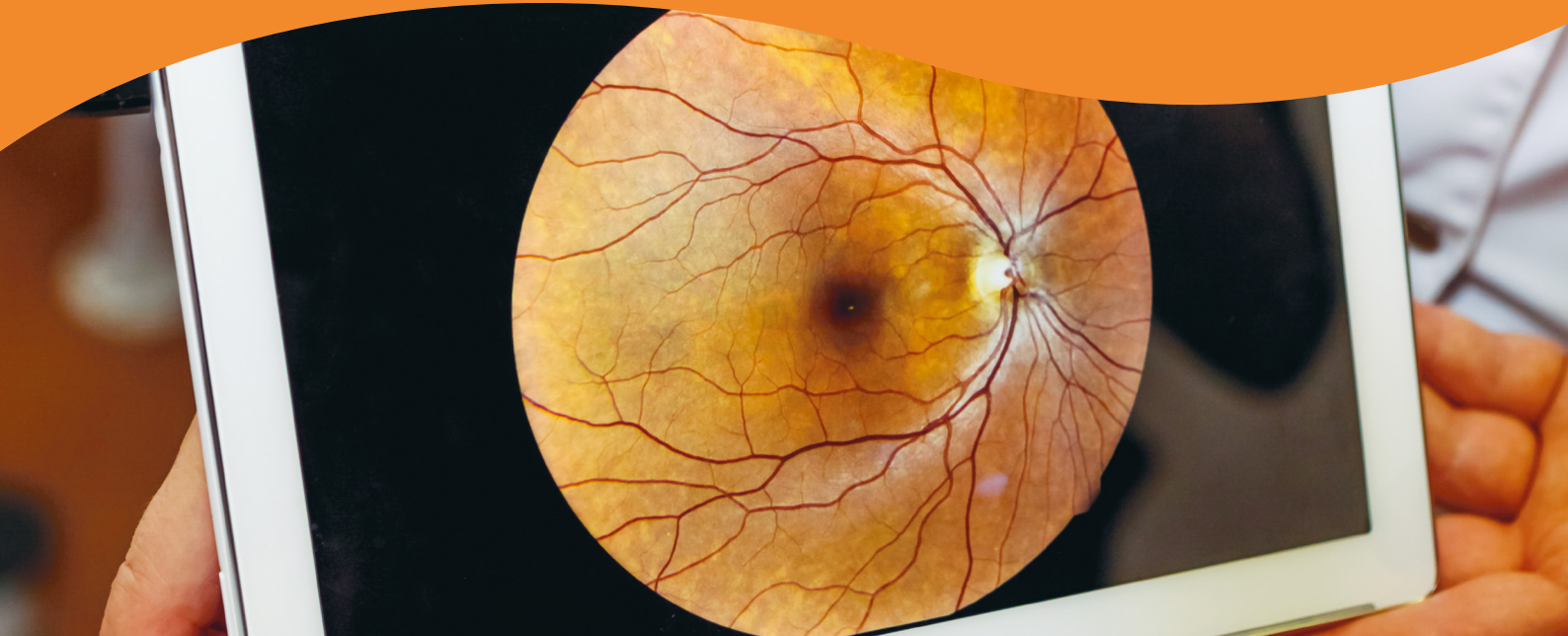




Developing a human retina model to understand and diagnose Alzheimer's disease



What is the focus of the research?

To discover if studying the retinas of people with Alzheimer's disease can be used to understand, and develop treatments for, the toxic build-up of a brain protein called amyloid beta that causes cognitive decline.



Why is it important?

The abnormal aggregation of amyloid beta is a hallmark of Alzheimer's disease. It forms plaques between the brain's nerve cells, which disrupt the complex cell-to-cell communication system. These plaques can appear decades before a person first experiences symptoms. Unfortunately, we still don't know why they appear or how to prevent their accumulation.

Our retinas, the light-sensing tissues in our eyes, are extensions of the brain. Post-mortem research has discovered similar levels of amyloid beta plaques in the brains and retinas of people with Alzheimer's disease. Importantly, these retinal plaques also cause neurodegeneration.

Despite these significant findings, studies on living people have not been performed because it's extremely difficult to obtain retinal tissue while people are alive. This has been a major barrier to developing new treatments for neurodegenerative diseases like Alzheimer's disease.

Thankfully, cutting-edge technology has made it possible to generate human retinal cells in a petri dish. A feature of these cells is that they retain a person's unique genetic information, so scientists can study how their genes predispose them to Alzheimer's disease.

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I am fascinated by the retina as a surrogate or complimentary model of Alzheimer's disease, because the eye is really the window to brain health. ”

— Dr Grace Lidgerwood

In this project, Dr Lidgerwood will generate retinal cells from the stem cells of people with Alzheimer's disease and study them in real-time throughout the duration of disease. She will be on the lookout for undiscovered molecular pathways that cause the toxic build-up of amyloid beta.

If successful, Dr Lidgerwood will create the first lab-based retinal model of Alzheimer's disease, which will be used to help discover drugs that can prevent or reverse amyloid beta plaque damage in the retina. Dr Lidgerwood hopes that the results of this project may pave the way for non-invasive retinal examinations to become part of the Alzheimer's disease diagnostic process.



How will this happen?

Stage 1: use a cellular model to assess the impact of Alzheimer's disease on the retina pigment epithelium using patient-derived stem cells with mutations in amyloid pathways.

Stage 2: assess the effects of any pathology on the retina related to the Alzheimer's disease mutations.

Stage 3: monitor biomarkers of Alzheimer's disease in real time by tracing the molecular changes that occur over 3-6 months in the cellular model.



How are human cells generated in a dish?

Scientists begin the process by taking a small biopsy of a patient's skin or a blood sample. These cells are then grown in the lab and can be reprogrammed into pluripotent stem cells.

Pluripotent stem cells can become any cell type of the human body (through a guided process called differentiation), including those affected by disease, while still retaining the person's genetic information. Scientists use this process to detect cellular pathways that are dysregulated by disease, essentially creating a patient's very own disease model in a dish.



What will this mean for the future?

- A retinal cell model of Alzheimer's Disease that could be used in biomarker discovery.
- Hope of early detection of Alzheimer's Disease using retinal examination.



Who's undertaking the research?

Dr Grace Lidgerwood, University of Melbourne

Dr Lidgerwood is an early career research fellow in the Department of Anatomy and Physiology at the University of Melbourne. Since receiving her PhD in 2018, Dr Lidgerwood has expanded her skills in stem cell research to create more complex and biologically relevant models of neurodegenerative diseases that affect the retina.

She has raised more than \$1.5 million in competitive research funding for her team and published 21 peer-reviewed papers in high-impact journals, including *Nature Communications* and *Cell Genomics*. She is the former chair of the Australian Society for Stem Cell Research, which is an early career researcher subcommittee and the central stem cell organisation within Australia.

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The title of Dr Lidgerwood's project is *Modelling Alzheimer's disease using a novel stem cell model of the human retina*.