Seeing more clearly

Degenerative eye diseases affect millions of people around the world, causing progressive loss of vision and, in some cases, complete blindness. Researchers in Australia are using stem cell technologies to investigate ways of halting, or even reversing, the effects of common eye diseases.

CENTRE FOR Eye Research Australia

The Centre for Eye Research Australia (CERA) was established in 1996 to investigate both the causes of and possible treatments for eye diseases, combining population health and clinical epidemiology with advanced laboratory studies. Based at the Royal Victorian Eye and Ear Hospital in Melbourne, CERA's Neuroregeneration Research and Clinical Genetics Units are investigating potential treatments for blinding diseases – such as glaucoma, age-related macular degeneration (AMD) and inherited retinal dystrophies – using induced pluripotent stem cells (iPSCs) to generate cellular models of disease.

Associate Professor Alice Pébay, Head of the Neuroregeneration Research Unit, explained: "Obtaining ocular tissue samples from living patients has historically been a barrier to developing new treatments for blinding diseases. The advent of techniques allowing the generation of iPSCs from adult tissue has been a major breakthrough, providing powerful new tools for disease modeling. Using these methods, we can now derive iPSCs directly from patient biopsies, then differentiate them into specific retinal cell types to create *in vitro* models of the ocular condition of interest. This enables us to study the complex genetics and molecular mechanisms of diseases such as glaucoma and AMD and, equally importantly, undertake large-scale drug screening programs to find potential cures."

The group uses the protocols developed by Yamanaka and colleagues to reprogram somatic cells taken from skin biopsies of individual patients, generating iPSC lines which form the basis of their research. "Once we had successfully created patient-derived

The large-scale disease modeling team at CERA

stem cell lines, we needed to establish robust protocols for the maintenance of our cell cultures," Alice added. "This is a fairly labor-intensive and time-consuming process and, because our intention was to undertake large-scale studies – looking for potentially very small drug effects that might halt the progression of these pathologies – it was not practical to continue performing this manually. Automation was clearly the way forward, and would also help to minimize the variability between cell samples, giving us greater confidence that our protocols would be reliable enough to detect even small changes in cellular behavior."

> "We've made more iPSC lines in the last few months than we had over the preceding couple of years."

Associate Professor Alex Hewitt, Head of Clinical Genetics, continued the story: "Our main aim for automation was to free up staff time and standardize the cultures we produced as much as possible. There was no off-the-shelf solution on the market that met all our requirements, and so we approached the Tecan Integration Group (TIG) through our local Tecan offices to create a bespoke Freedom EVO® system offering sterile working conditions and an integrated 84-plate LiCONiC incubator. As with any new venture, it took us some time to develop a culture maintenance protocol robust enough for use with our iPSC lines, but it is now working well, allowing us to generate large quantities of cells for our research. In fact, we've made more iPSC lines in the last few months than we have over the preceding couple of years."

The automated platform and the associated offline equipment were acquired thanks to generous donations from the Joan and Peter Clemenger Foundation and the Phillip Neal Bequest. Alice continued: "Our next task is to create protocols to efficiently passage and differentiate the iPSCs into the patient-specific cell types of interest to our research; retinal pigment epithelium cells – which are dysfunctional in AMD and inherited retinal dystrophies – and retinal ganglion cells, which are affected in glaucoma and other optic neuropathies. This work is also being performed on the Freedom EVO, with the aim of generating and maintaining the large quantities of fully differentiated cells we require for our disease modeling and drug screening programs."

"Our ultimate goal is to find solutions for major blinding eye diseases that affect Australians, and to pioneer vision regeneration programs to give hope to people who have lost their sight. Very few labs globally are equipped to perform this type of work, and we hope that this approach will lead to new targets and novel therapies for the prevention and treatment of common and devastating diseases. It's very exciting," Alice concluded.

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