MacularNEWS

Autumn 2021 : Edition 22

Professor Gillies (second from left) and Dr Zhu (second from right) with the team.

Using New Technologies to Treat Macular Degeneration

Scientists in the Macula Research Group are exploring new ways to treat macular degeneration using the same mRNA (messenger ribonucleic acid) technology that created the COVID-19 vaccine.

A year ago, Professor Mark Gillies and Dr Ling Zhu decided to try packaging RNA coding molecules inside lipid nanoparticles ("nano" means super tiny) to treat macular degeneration. The lab is building a state-of-the-art platform using four advanced nanotechnologies to prevent blindness.

Director's Message

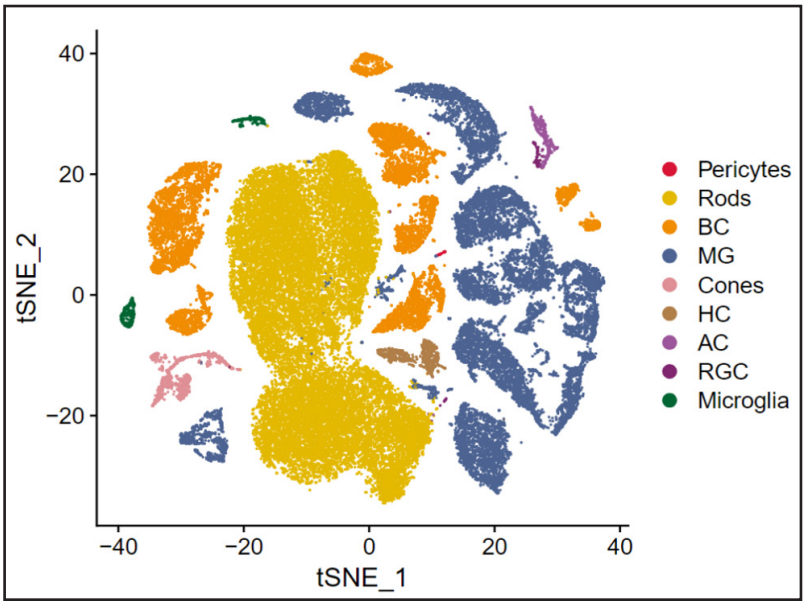
In this issue of MacularNEWS, we look at our latest clinical laboratory research into potential treatments for macular degeneration. Research into new treatments is vital to ensure that we reduce the impact of age-related macular degeneration, which is one of the most common causes of vision loss worldwide.

Professor Mark Gillies
Macula Research Group

1. Using advanced single-cell RNA sequencing to screen for new drugs

Single-cell RNA sequencing can detect molecular changes in individual cells. We have successfully established this cutting-edge technology in the Gillies Lab to understand how retinal diseases develop and how treatments affect every single retinal cell. This will increase the number of experimental treatments we can test in animal models and human retinas, as explained below.

Figure 1: Transcription pattern from 80,000 retinal cells with single-cell RNA sequencing. mRNAs from individual cell types are grouped by colour. It is easy to see, for example, if a drug that is being tested switches on or off the production of target retinal proteins in the cells of interest using this method.



2. A robust in vitro transcribed (IVT) mRNA synthesis platform

Gene therapy transfers genetically modified materials (payloads) into a patient's tissues or cells to correct the abnormal gene contributing to a particular disease. mRNA has been used increasingly in gene therapy in recent years due to its unique features. It has also been used to make the COVID-19 vaccine. Advanced mRNA gene therapy technology has higher efficiency than other payloads, so it is effective within hours. It has a better safety profile with less risk of causing cancer by damaging other genes. It is easier to standardise and scale up for biomanufacturing. We have established an mRNA synthesis platform that will help us screen for drugs that act on new therapeutic targets within weeks.

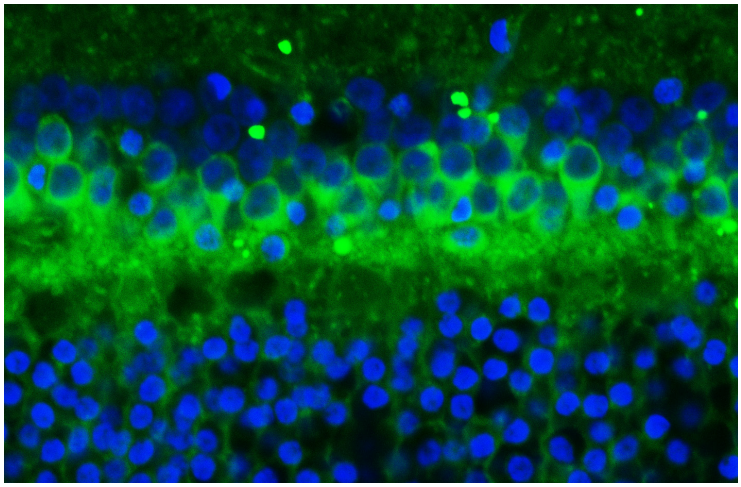
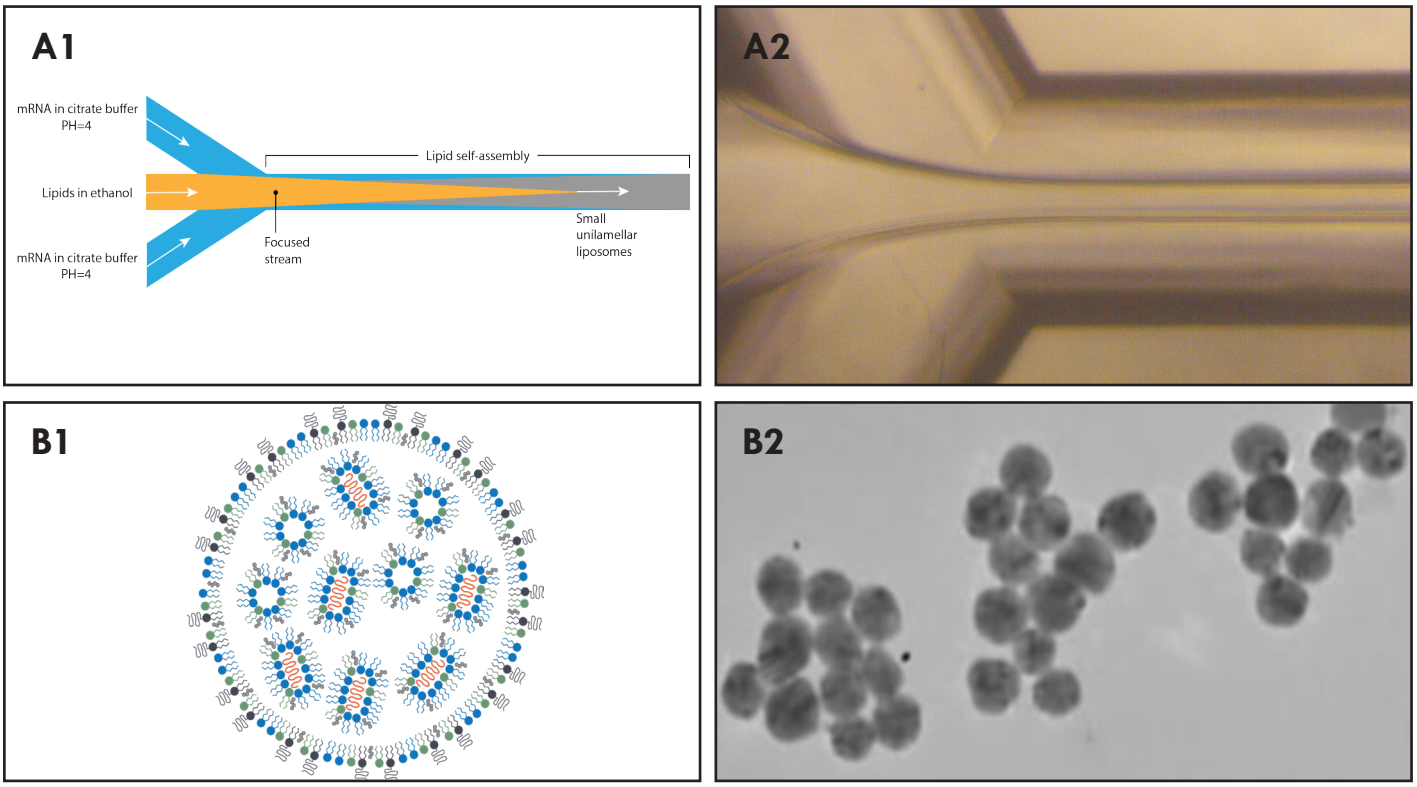


Figure 2: The expression of eGFP protein (the green colour) within the human retina transfected by eGFP mRNA.

3. An advanced microfluidic system to synthesise nanocarriers

Nobody thinks that making lipid nanoparticles (LNPs) reproducibly in the lab is easy. We have built a nanomedicine synthesis platform using advanced microfluidic technology to incorporate mRNA into lipid nanoparticles that are preferentially absorbed by different retinal cell types. We plan to develop the next generation of mRNA carriers that will specifically target the cells within the eye that need the treatment. Our technology is environmentally friendly since drug carriers are formulated from natural fats. The use of our advanced microfluidic system will ensure the quality of the synthesised lipid nanoparticles and allow the high yield production that is desirable for clinical applications.

Figure 3A1-2: A schematic of micromixing mediated LNPs production.
B1-2: A schematic of the mRNA wrapped with LNPs. The blue colour is the lipid and the orange colour is the mRNA.

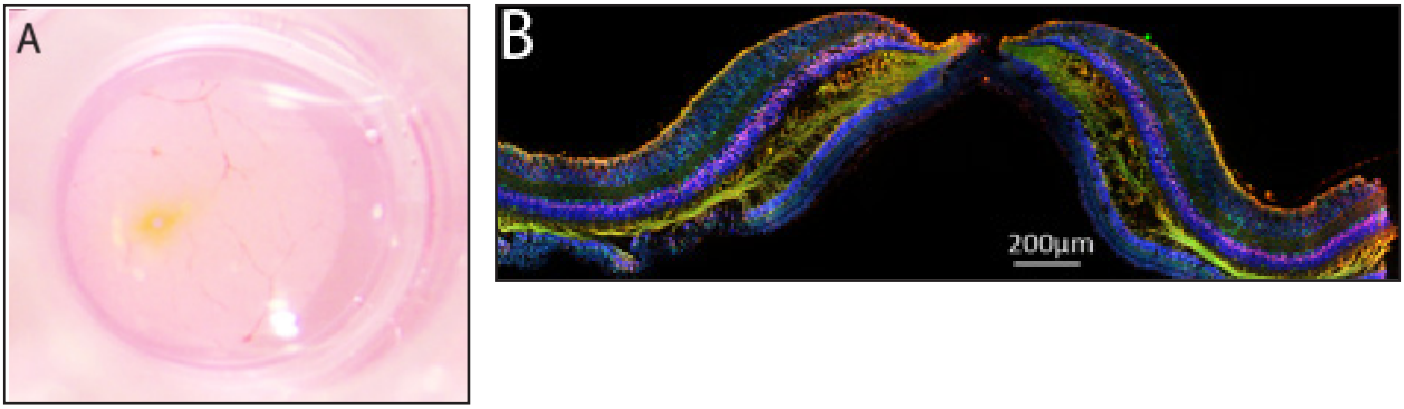


4. "Explants" of donated human maculas cultured in the lab

Human and mouse retinas differ in many respects. Only humans, primates and birds have maculas. Treatments effective in animal models of retinal diseases often fail in clinical trials due to this difference. We have established a unique way to grow donated human retinas in a dish for up to a week. We hope that this will narrow the translational gap, which is said to limit the translation of lab research into the clinic.

Our model preserves cell-to-cell interactions within the human retina and precisely reflects responses that would occur in living human retinas. Scientists will have a much better idea of what will work in humans using this model than they would if they only had data from animal models.

Figure 4A: Our unique human explant system.
B: The unique physiology structure of human macula, which does not exist in mouse retinas.



GLOSSARY

Lipid nanoparticles: Tiny fat droplet that carries the cure component.
Microfluidic technology: Using super tiny pipes.
mRNA (messenger ribonucleic acid): A molecule that tells a cell's protein-making factories what to do.

If you would like to make a tax-deductible donation or discuss leaving a bequest to support macular research please visit our website **sydney.edu.au/medicine/eye**, call us on **(02) 9382 7309** or post a cheque to: Save Sight Institute, South Block, Sydney Eye Hospital, 8 Macquarie Street Sydney NSW 2000 made out to 'The University of Sydney'

Save Sight Institute is a centre of The University of Sydney.

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