# MacularNEWS

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## Macula-on-a-Chip (MoaC) system

Like age-related macular degeneration, macular telangiectasia type 2 (MacTel) mainly affects the macula so it causes loss of central (reading, driving) vision. The absence of effective models to study the human macula has hindered our progress in understanding and treating macular diseases for many years. Our research is poised to change that.
We have developed a unique system to study macular disease as an alternative to using animal models which are not very helpful because laboratory animals generally do not have maculas. We have been able to revive human maculas which have been provided by eye donors after they have died. This “Macula-on-a-Chip (MoaC)" system allows us to study for the first time the responses of macular tissue to the stresses that we believe lie at the root of macular disease.

We have been particularly interested in the role of 1-Deoxysphingolipids (1-deoxySL) in MacTel. These unusual fats, which are made in many macular diseases, are toxic to retinal cells.
Our mission is to use our MoaC system *(Figure 1)* to simulate the impact of 1-deoxySL on human retinal cells, especially retinal cells in the macula, to reflect what happens in MacTel.

## Director's Message

In this issue of **MacularNEWS**, we highlight the laboratory's new technology "Macula-on-a-Chip" and the progressive research it has allowed to take place.

Thank you for your continued interest in our work. I hope you enjoy reading this issue.

**Professor Mark Gillies**
Macula Research Group

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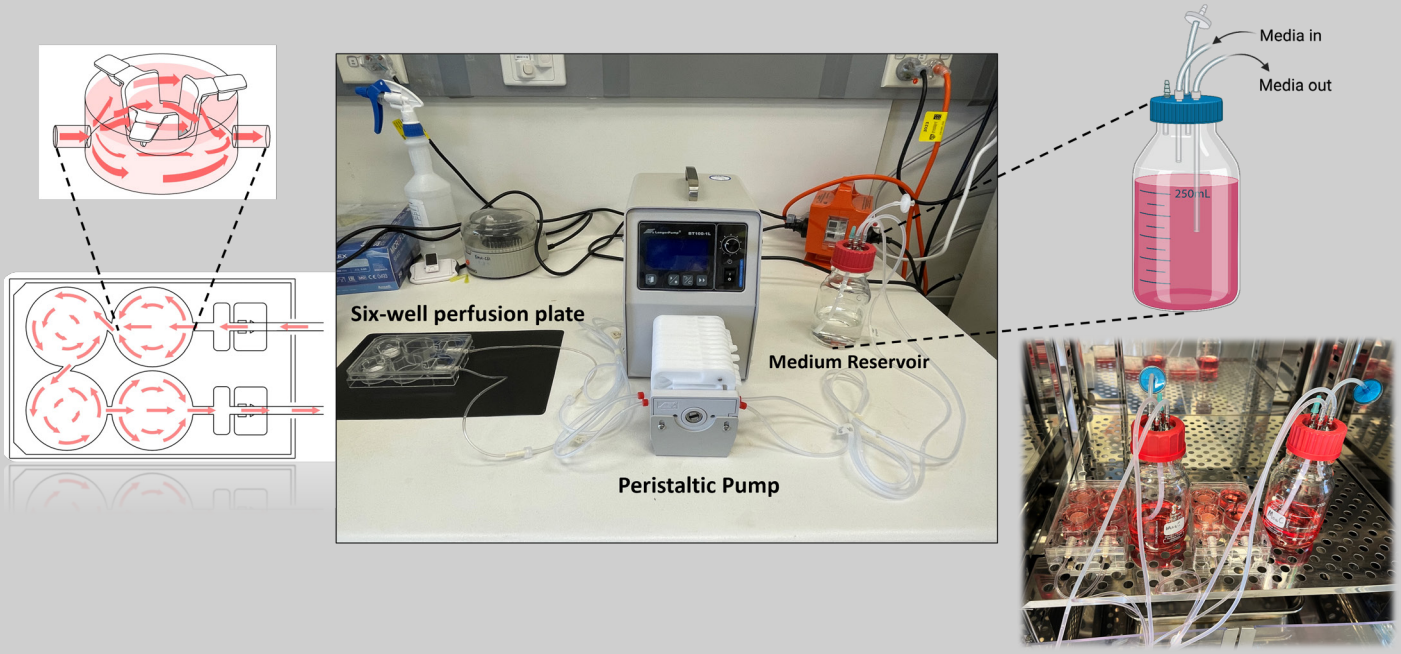


**Figure 1:** A window into the eye's inner workings - the MoaC system

*This diagram presents the MoaC system, our laboratory's pioneering technology, which creates a lifelike environment for studying the human macula. At its core is the perfusion culture plate, where living retinal tissues are sustained within individual wells, mirroring their natural conditions. Transwell inserts, seen here as circular elements, are placed within these wells to support the tissue cultures. The 12-channel pump circulates culture medium across these cultures, akin to blood circulation in the body, providing a steady flow of nutrients. On the right is the sterile medium supply, a customised bottle that ensures a continuous stream of nourishment for the cells. This entire setup is housed within a 37°C incubator, an environment that closely resembles the warmth and CO2 levels of the human body that are crucial for maintaining the health of the macular samples.*

This research begins with a delicate procedure of acquiring human retinal explants—precious tissues generously donated for research. These samples from the macula and peripheral retina are placed in a special medium that flows continuously. Over three days, we expose these samples to 1-deoxySL, observing its toxic effects. Our suite of techniques, including TUNEL staining for dead cells and other assays of cell health, helps us assess cellular and genetic responses to 1-deoxySL.
The journey of discovery has been enlightening. When the macular cells faced 1-deoxySL, they showed signs of distress, suggesting why MacTel mostly affects the macula. The macula's response was different from the rest of the retina, with many more genes from the macula responding to the toxin and more macular cells dying.

Our exploration goes beyond mere observation; we are also looking for new treatments. Nicotinamide Mononucleotide (NMN), a precursor of NAD, has emerged as a promising candidate. NAD (Nicotinamide adenine dinucleotide) is required for cells to generate energy that keeps them healthy.

When introduced to the stressed cells, NMN partially shielded them from the harmful effects of 1-deoxySL *(Figure 2)*. This paves the way for potential treatments that could fortify the macula against the onslaught of MacTel. However, the complexity of the human eye remains a challenge, and our work is far from complete.

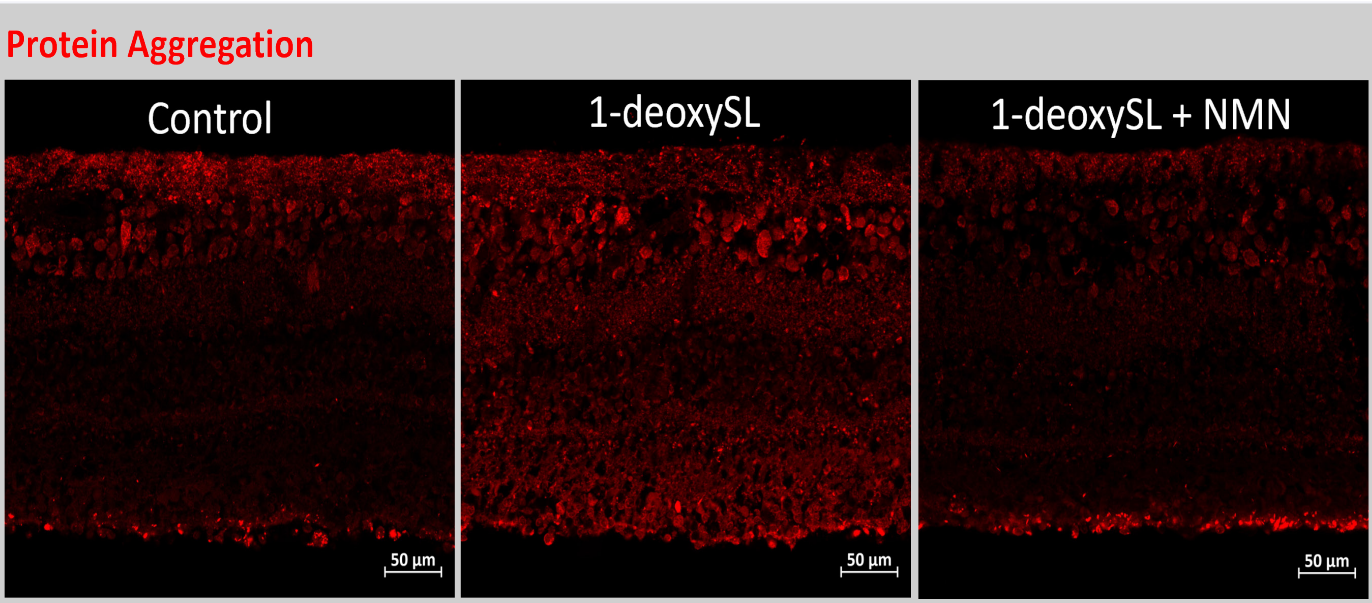


**Figure 2:** Visualising the protective effects of NMN on retinal cells

*These photographs show the response of human retinal cells to different treatments. The red staining indicates protein aggregation, a process that can be detrimental to the health of retinal cells. In the first image, the 'Control', we see a baseline level of this red staining under normal conditions. The middle image, exposed to 1-deoxySL, exhibits a marked increase in aggregation, signalling a stress response within the cells.*
*However, the final image offers a stark contrast: when treated with NMN, the retinal cells have much less protein aggregation (red staining). This reduction indicates that NMN may effectively diminish the harmful protein aggregation caused by 1-deoxySL exposure, suggesting a therapeutic potential for improving retinal health.*

As we conclude this phase of our research, we reflect on the strides we have made. Our study has provided significant insights into the pathogenesis of MacTel and laid the groundwork for potential treatments. The MoaC system allowed us to observe the cellular impact of 1-deoxySL, bringing us closer to understanding why the macula is particularly susceptible.

Moving forward, we will validate our findings at the protein level and evaluate the protective effects of NMN more extensively. Each experiment is a step towards unravelling the intricacies of MacTel further, with the ultimate goal of preserving sight.

The engagement and participation of our supporters and patients in our research efforts motivates us and fuels our progress. Together we continue to push the boundaries of understanding and treatment, hoping to safeguard the gift of sight for future generations.

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'

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