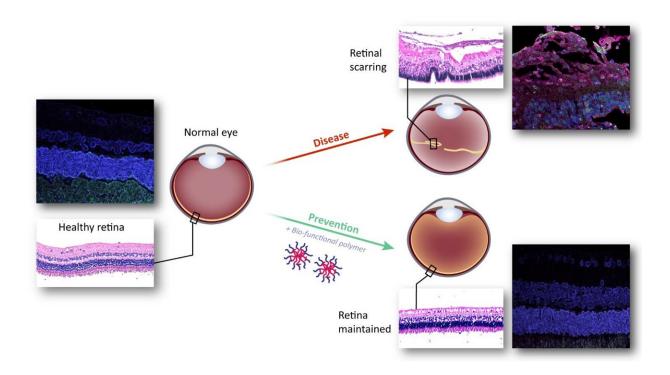


A novel therapy using unique thermogel prevents retinal scarring

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A healthy retina contains organized light-sensitive layers of neurons at the back of the eye. Upon retinal scarring, it can result in retinal detachment with loss of these organized layers and visual impairment. Application of a bio-functional thermogel prevents this detachment and maintains the retina. Credit: Kim Chi Tran, A*STAR's Institute of Molecular and Cell Biology (IMCB).

Singapore scientists have developed a bio-functional thermogel, a type of synthetic polymer, to prevent retinal scarring caused by failed retinal



detachment repair surgery. Proliferative vitreoretinopathy (PVR) occurs when the retinal scarring prevents the retina from healing and falling back into place, and accounts for more than 75 percent of failed retinal detachment surgeries, and may result in vision loss or blindness if left unrepaired.

Current treatment options for PVR are limited to surgical removal of these scar membranes with guarded visual recovery. This work highlights the potential of using synthetic polymers alone to modulate cellular behavior and for the first time, offers a novel thermogel-based therapy to prevent retinal scarring. The team behind the development hails from A*STAR's Institute of Molecular and Cell Biology (IMCB) and Institute of Materials Research and Engineering (IMRE), the National University of Singapore (NUS) and the Singapore Eye Research Institute (SERI).

The research team demonstrated that a bio-functional thermogel alone is able to prevent retinal scarring in a pre-clinical model that mimics human.disease. Using retinal cells, the team observed that the thermogel prevented the development of the scar membranes by modulating cellular behaviors such as proliferation and migration. Using genome-wide transcriptomic analysis to profile cellular gene expression, they revealed that the thermogel activated a protein called nuclear factor erythroid 2-related factor 2 (NRF2), to kickstart a series of chemical reactions to prevent scarring.

"Our study offers insight into how <u>synthetic polymers</u> no longer function merely as inert drug carriers. It challenges the conventional belief that the use of a small molecule drug is always required to achieve a therapeutic effect. Beyond ophthalmology, this unique bio-functionality of the thermogel can also be applied to other diseases such as orthopedics where intra-articular joint scarring might be a problem," said Dr. Su Xinyi, Senior Principal Investigator and Division Director at



A*STAR's IMCB, and Assistant Professor in the Department of Ophthalmology at NUS Yong Loo Lin School of Medicine.

"When we first developed this bio-functional thermogel at IMRE, we realized it was a significant step forward in developing next-generation biodegradable polymers. Its ability to mimic and substitute vitreous given the biocompatibility of the material, makes it useful for many other biomedical applications," said Prof Loh Xian Jun, Executive Director at A*STAR's IMRE.

The thermogel is currently being commercialized by Vitreogel Innovations Inc, an A*STAR spin-off that focuses on developing polymer-based therapeutics for ophthalmology indications. Vitreogel Innovations Inc is an ISO 13485 (Medical Device Quality Systems) accredited company that is generating a clinical grade version of the polymer for first-in-man clinical trials.

Building on this work, the team will continue to test the safety and efficacy of this polymer for retinal detachment repair and PVR prevention using additional pre-clinical disease models. Through their work, the team aims to engineer the next generation of polymers with targeted chemical modifications to elicit specific cellular behaviors, and identify alternative applications of the thermogel beyond ophthalmology.

The research was published in *Nature Communications*.

More information: Bhav Harshad Parikh et al, A bio-functional polymer that prevents retinal scarring through modulation of NRF2 signalling pathway, *Nature Communications* (2022). DOI: 10.1038/s41467-022-30474-6



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