Gift of SIGHT

November 2025 NEWSLETTER

Dear friends and supporters,

My thanks to those of you who generously sponsored Ian Moran, Andrew Bateman, Peat Allan and myself in the Clarendon Marathon in October. Running as a relay team, we raised an amazing £1,492.

Since September, I've had the privilege of speaking about our work on intermediate macular degeneration at the European Eye Epidemiology Consortium meeting in Dijon, and also at the International AMD Genomics Conference in Edinburgh.

Over the past few months, we have published several papers from our ongoing PINNACLE trial, which I lead, studying intermediate age-related macular degeneration (AMD). Using adaptive optics (a special imaging technology similar to that used by the Hubble Space Telescope), we captured highly detailed pictures of tiny areas of inflammation in the eyes of people with AMD. Our findings from this study were published in the journal *Eye* in October.

In August, we published a paper in *NPJ Digital Medicine* on training computers to analyse retinal images, helping clinicians assess the severity of macular degeneration.

Another paper is being finalised on clarifying features that predict AMD progression when a person starts to develop early stages of the disease. This should allow us to prioritise patients most at risk, so that they receive a more urgent follow-up. To achieve this, we have reviewed thousands of patient visits to ensure the data collected is accurate. We plan to present the outcomes of this work at the Association for Research in Vision and Ophthalmology (ARVO) meeting in May 2026, and submit it for publication in a leading eye journal. Overall, we have published over 20 papers this year, with several more in progress, demonstrating the high standard of work being undertaken in our laboratories.

In clinical trials, we are currently assessing new treatments for an inherited eye condition called Stargardt disease and for diabetic eye disease. We are also setting up trials for central serous chorioretinopathy and dry AMD, which will begin in early 2026. It's always reassuring to know that these trials are underway, some of which may lead to improved or new treatments for patients.

Gift of Sight has recently received an amazing legacy from a local couple who sadly passed away in 2023 and were grateful for the care given at Southampton Eye Unit. We will, of course, keep you informed about how this generous gift will be used. As mentioned in our last newsletter, we have included reports from two members of our group who have benefited from legacy gifts. The kindness of our donors is truly humbling.

As we approach the festive break, I wish you all a peaceful and happy time.

With my warmest regards.

Andrew Lotery

Andrew Lotery MD, FRCOphth
Professor of Ophthalmology
University of Southampton

Dr Jörn Lakowski, Associate Professor

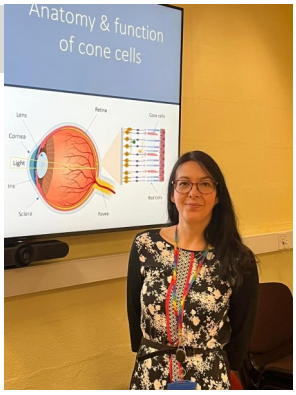
There are two central questions in ophthalmic research: *How does the human retina, with its complex lamination and intricate connectivity, form during development, and how is it maintained in adulthood?* While these questions may seem basic and are often overlooked in the competitive, therapy-oriented funding mechanisms of modern academic research, the answers underpin the creation of effective therapies for many currently incurable retinal diseases. In other words, if you do not understand how something works, it will be very difficult to fix it if it is broken.

For over a century, scientists have tried to answer these questions, but despite much progress in recent decades, many details remain unresolved. For example, we only recently started to appreciate that photoreceptors - the light-sensing cells in the retina - undergo extensive migration during retinal development. This turned out to be a critical process, as failure to migrate prevents the cell from taking up the correct position in the mature retina, leading to visual defects. Interestingly, it is this migratory ability that we try to exploit when using photoreceptors in "cell replacement therapy" to treat inherited retinal dystrophies such as retinitis pigmentosa. This approach involves transplanting lab-grown photoreceptors into the retina to replace those lost to disease, thus preventing further visual decline. After transplantation, donor cells must negotiate the new environment, making the correct turns to take up their appropriate positions and forming functional synaptic connections with other cells. How exactly newly formed photoreceptors accomplish this remains unknown; however, it is clear that a better understanding of this natural process would allow us to reproduce and steer the cells' migratory ability in future clinical applications.

Over the past two years, we have used human pluripotent stem cell-derived retinal organoids - human "mini-retinas" - grown in our Gift of Sight-supported stem cell lab as a model system to dissect the mechanism of cone photoreceptor migration. This was supported by a grant from the Biotechnology and Biological Sciences Research Council (BBSRC). Using sophisticated bioinformatics (big data) and genome-editing approaches, we have identified what we believe are several key regulators of cell migration in the developing retina. Furthermore, in collaboration with the Biological Imaging Unit of the Faculty of Medicine, we have utilised a newly established "spatial transcriptomics" setup, allowing us to visualise the activity of up to 6,000 individual candidate genes in our "mini-retinas". Combined, this work has generated exciting new data, and we are now working towards finalising our findings for publication in specialist academic journals. During the last year of this grant, we will focus on identifying chemical reagents, or drugs, which we can use to facilitate migration and synapse formation of transplanted donor cells in a future clinical setting.

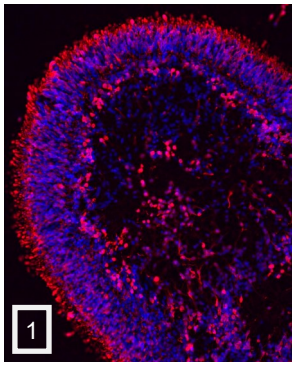
The unwavering support from the many Gift of Sight supporters has once again proven essential to the success of this project and to all the other research being conducted in our stem cell lab.

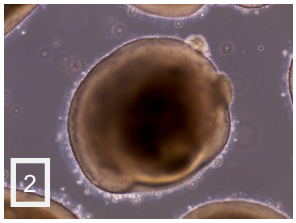
Catherine Robertson, PhD Student



Thanks to a generous legacy donation to Gift of Sight, I was able to undertake a three-year PhD project exploring cone photoreceptor development. An essential step toward creating targeted treatments for vision loss lies in the ability to better understand the biological mechanisms that govern retinal development. Photoreceptors, the light-sensitive cells in our eyes, come in two types: rods and cones. Understanding how these cells develop is key to unlocking therapies that could one day restore sight.

Our research focused on a little-known protein called GNGT2, which is involved in the phototransduction pathway - the process by which light is converted into signals the brain can interpret. Early studies hinted that GNGT2 might play a role in cone development, and we were therefore keen to understand whether it had additional functions during eye formation.





To do this, we developed what is known as a "knock-out" cell line, where a specific gene - in this case GNGT2 - is removed or silenced. We used a gene-editing tool called CRISPR, which acts like a pair of molecular scissors due to its ability to cut or edit specific regions of DNA. GNGT2 was successfully edited in a human embryonic stem cell line, halting the production of the protein in the modified cells.

From these cells, we grew retinal organoids, which are tiny lab-grown structures that mimic the development of the human retina. By comparing cone development in our knock-out models to normal controls, we discovered that GNGT2 does indeed play multiple roles in the retina. And we found that an absence of GNGT2 led to a reduced expression of proteins critical for cone cell formation, revealing a previously unknown layer of complexity in cone development. We're excited about where this journey could lead next.

1. Sectioned retinal organoid after 250 days in culture. Photoreceptors are shown in red, and nuclei are counterstained in blue. 2. Bright field image of a retinal organoid after 250 days in culture.

Dr Eloise Keeling, Senior Research Fellow

I have now been working with Dr Jay Self for four years. During this time, I have refined a cell culture model of a common form of albinism and used this to screen almost 1,000 Food and Drug Administration (FDA)-approved drugs to try and identify new treatments. Because these compounds are all FDA-approved, the safety studies are already completed and could, therefore, reach patients more quickly. We discovered a few drugs that seem to work really well and have studied them in depth to understand their chemical binding and biological effects. From this, we have one top candidate drug that works well on a range of albinism mutations. We have submitted a patent application for the use of this drug as an albinism treatment and have written a subsequent manuscript, which is currently being peer-reviewed.

We are now testing the drugs in both eye cells and skin cells to provide more evidence of the drug working, to support both the patent application and for future clinical trial funding.

RETeval handheld testing device

Alongside this, I was also involved in a small project using a handheld electrodiagnostic testing device (EDT) to evaluate its suitability to speed up albinism diagnosis, rather than patients having to wait for full EDT testing, which has about a four-month waiting list. Since albinism treatments have to be given to babies within their first 18 months, it is important that we are able to diagnose patients quickly and efficiently, to give them the longest treatment window possible. This work has been published in the academic journal *MDPI Diagnostics*. We are now in the process of preparing a follow-up paper looking at detection of visual field defects in a variety of neurological conditions, for example strokes, and eye diseases including glaucoma and retinal disorders.

I am grateful to all Gift of Sight donors who have helped my research studies in many ways, including contributing to my salary over the past three years. Thank you.

OUR THANKS...

Congratulations to Ben and Alex from the Alma Inn, Upham, Southampton who climbed Mount Snowdon on 25th August. Their incredible effort has already raised £555, and generous patrons continue to support us with ongoing donations.

Warm wishes to **Paul Moulin,** who celebrated his 80th birthday by asking for donations instead of gifts - raising £220. Thank you for your generosity Paul.

Our **Bonfire Night Bake Sale** went off with a bang at the entrance of University Hospital Southampton, raising £551. It was lovely to see familiar faces, including staff and patients. Thanks to everyone who came and supported us.

A heartfelt thank you to **Karen and Paul Larcombe**, their daughter Nicole, and son-in-law Andy, who walked 12 miles of the Test Way raising an amazing £959. Their contribution will help our paediatric team continue vital research into nystagmus.

Huge thanks to **Vickie Lush** who organised a fantastic quiz night near Winchester, raising an impressive £2,630 to support our AMD research. Quizmasters Glenn and Debbie kept the evening lively, while Vickie and Mary coordinated hotdogs and cupcakes for over 90 guests. The event also celebrated the birthday of Vickie's mum Val, whose sight has been preserved thanks to years of treatment.

Christmas Card packs are available from our online store. Our thanks to the generous artists who have provided us with lovely cards over many years. The link to buy is on the events page of our website.

UPCOMING EVENTS IN 2026: Full details at www.giftofsight.org.uk/events

Bach with Brass, 1st February, St Pauls Church, Winchester, 4pm. £20 per person.
We're thrilled to be working again with Jon Newman and Andrew Hayman for another wonderful performance by Bach Winchester Voices and Orchestra. The programme will include three Bach cantatas from Sonn & Schild, featuring amazing soloists and brass instruments. Professor Lotery will give a short talk before the performance. Tickets are on sale now.

Little Court Garden Party, 11th June, Little Court, Crawley, Winchester, 6pm. £20 per person.
Join us for a delightful summer evening with fizz, canapes, and a talk from Professor Lotery. You'll have the chance to mingle and chat with some of our vision research team in the beautiful garden at Little Court, thanks to the generosity of Mrs Patricia Elkington.

Professor Lotery's Big Birthday! Professor Andrew Lotery is celebrating a rather special birthday in December 2025 and has kindly asked for donations to Gift of Sight in lieu of gifts. If you would like to honour the occasion, please donate and mention 'Prof Birthday' as your reason for giving.

Can you help? Do you know a local business that may like to support our events - either through sponsorship in return for promotion, or by donating raffle prizes? We'd love to hear from you!

Contact: Ailsa Walter | T: 023 8059 9073 or Jennie Mugridge | T: 023 8059 5921
Email: info@giftofsight.org.uk Website: www.giftofsight.org.uk

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