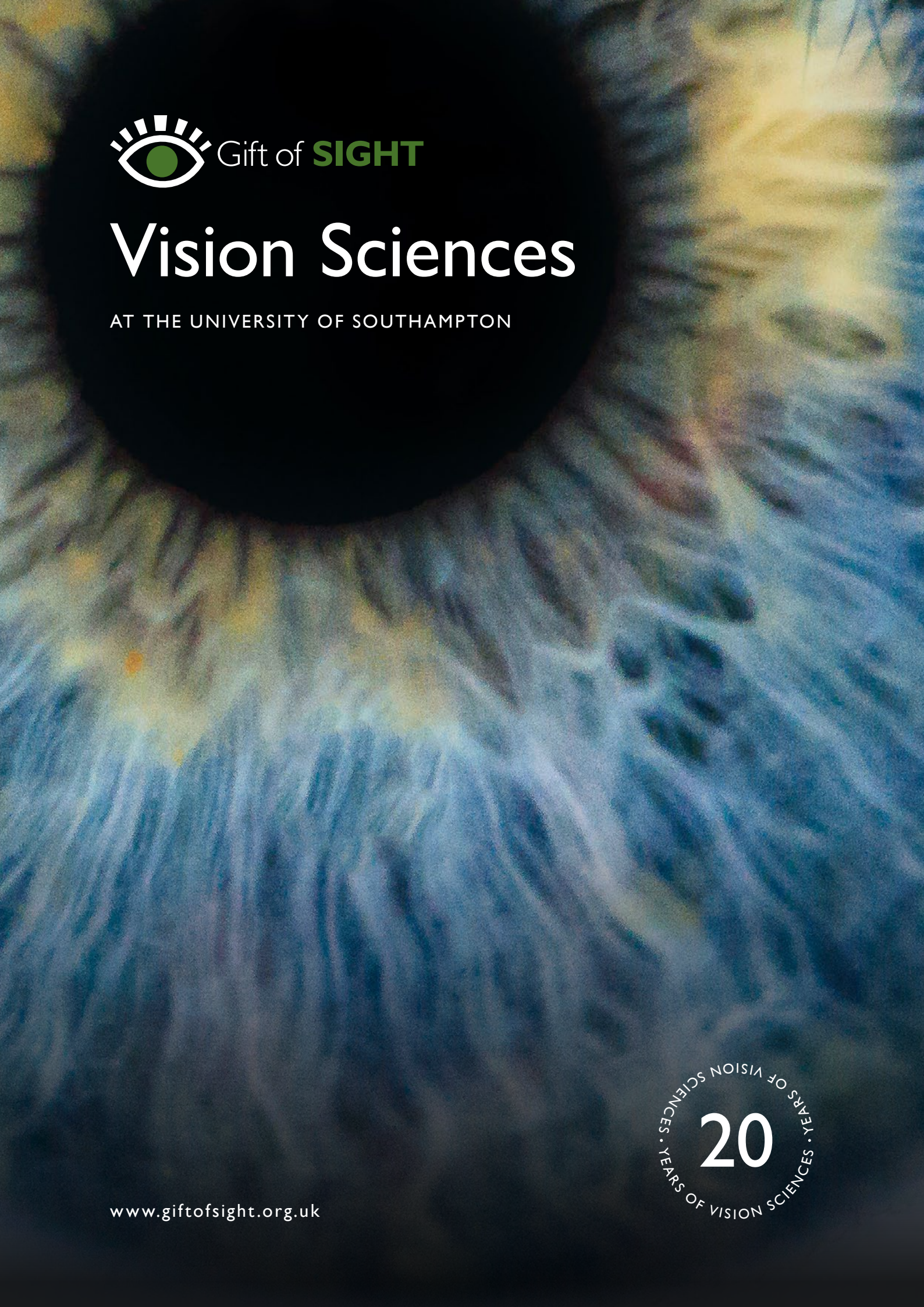

Gift of SIGHT
Vision Sciences
AT THE UNIVERSITY OF SOUTHAMPTON
20 YEARS OF VISION SCIENCES • 20 YEARS OF VISION SCIENCES •
www.giftofsight.org.uk

Contents

Welcome

from the Dean

It gives me great pleasure as Dean of the Faculty of Medicine to write this foreword to this brochure celebrating 20 years of vision research at the University of Southampton.

The vision science group began with the appointment of Professor Andrew Lotery as the first University Chair of Ophthalmology in September 2002. Professor Andrew Elkington held an honorary Chair of Ophthalmology but this was the first investment by the University in an academic research group in Vision Sciences.

One of the great things about the Faculty of Medicine is that it is co-localized within University Hospital Southampton and this allows clinician scientists like Professor Andrew Lotery to truly adopt a bench to bedside approach to research. Being part of the research intense University of Southampton gives ready access to leading academic colleagues in other disciplines like engineering and computer science who contribute to our work, solving major disease challenges, bringing innovative approaches and new technologies to discovery science.

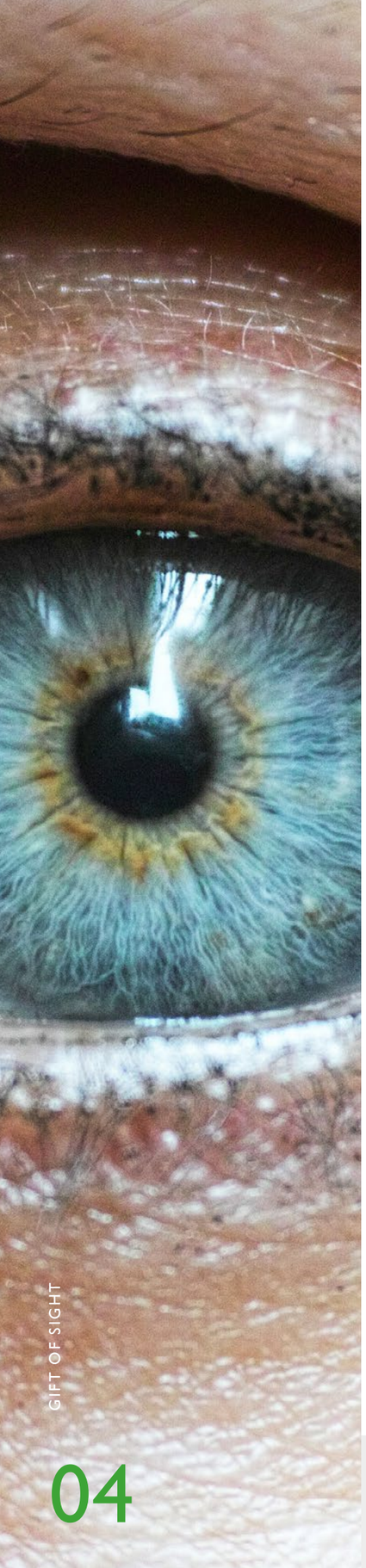
An important early development for vision science has been the banking of DNA samples from patients with common blinding diseases such as macular degeneration and glaucoma. This would not have been possible without the co-localization at the hospital site, allowing Andrew and his colleagues to engage with patients who contribute in this way to help research. Working in this way has led to many genetic insights into common causes of eye disease and this is now being translated into treatments e.g. gene therapy. Gene therapy trials are now underway for conditions such as macular degeneration.

Translation of basic science to therapeutic advances is key for the vision science group and this has been greatly helped by the University and Hospital's shared commitment to clinical research. A key component of this is the NIHR Wellcome Trust Southampton Clinical Research Facility located in University Hospital Southampton. This has allowed the vision group to build a dedicated group of research delivery focused ophthalmic doctors and research nurses, leading national and international clinical trials. Notable examples include two NIHR funded trials for central serous chorioretinopathy, a Medical Research Council funded trial for albinism and a Wellcome Trust funded trial for macular degeneration.

I am excited by what the group has achieved in the last 20 years. Growing from a single appointment to six tenured academic staff each leading vital research projects is a tribute to the energy and dedication of the team. I hope you enjoy reading about the group's achievements in this brochure and like me you will look forward to following their progress towards developing new treatments and therapies for patients in the futrure.

With best wishes,

PROFESSOR
DIANA ECCLES
Dean of Medicine



Goals and Vision for the Future

PROFESSOR ANDREW LOTERY

It is really hard to believe that 20 years have gone by since I was appointed as the first University appointed Professor of Ophthalmology. Initially the "Chair of Ophthalmology" was just that, i.e. a chair to sit on in a very small office and some lab space.

However, I discovered that there was a lot of goodwill and support in Southampton to help me get started. Firstly, a research grant from the Wessex Medical Trust and the Island of Guernsey allowed us to start genetic studies on age related macular degeneration (AMD). We travelled via ferry to Guernsey to collect blood samples from patients to study the genetics of macular degeneration on the island. This involved many late nights in the lab processing samples on our return from Guernsey. Interestingly we found some families where there seemed to be an autosomal dominant form of AMD. We subsequently discovered this was due to these patients having changes in the CFI gene and this research has helped develop a gene therapy for dry AMD which is now excitingly in clinical trials.

Another key event that happened at the same time was that the Wellcome Trust supported the creation of a clinical trial research facility in Southampton. This allowed me to utilise dedicated research nurses to also collect DNA samples from patients attending Southampton Eye Unit. These DNA cohorts now number several thousands of patient samples. We also started performing clinical trials.

One of our first clinical research nurses Marie Nelson is now R&D Head of Nursing and Health Professions in University Hospital Southampton. Another ophthalmology research nurse, Rebecca McKay, went on to become the Chief Operating Officer of the Wessex NIHR Clinical Research Network. Many junior doctors who worked in research with us have since successfully advanced to NHS Consultant or Clinician Scientist University posts.

Another key decision in 2002 was to restart the Gift of Sight charity appeal which has been so crucial for the development of our programme.

Over the last 20 years our work has tried to follow our Vision Science mission statement "To produce world class research to help alleviate blindness". We aimed to achieve this through our core values.

"Over the last 20 years our work has tried to follow our Vision Science mission statement:

To produce world class research to help alleviate blindness"

Our Core Values

Funding

Attracting sufficient funding to allow research to proceed quickly

Training

Training the next generation or academic ophthalmologists and visual scientists

Dissemination

Disseminating our research findings in leading research journals

Teamwork

Working as a team to achieve these goals

Mission Statement

To produce world class research to help alleviate blindness

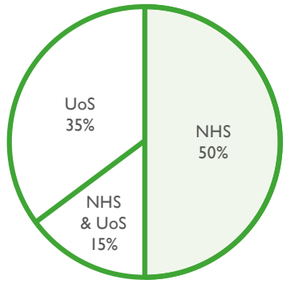
We have adapted our research to move with innovations in research and I am sure this will continue for the next twenty years and beyond. For example, our initial research was directed at finding genes that caused retinal diseases such as macular degeneration. This has been successful and we now have several candidate genes to test as treatments in clinical trials. We discovered that some of the families in Guernsey actually had mutations in the complement factor I gene. Gene therapy to rectify this defect is now being tested in clinical trials. I was excited to be able to support the development of these trials. We are also using artificial intelligence and machine learning methods to study hundreds of thousands of retinal images to better understand what makes macular degeneration progress. The computing power and techniques to do this did not exist until a few years ago. Dr Jörn Lakowski is leading our studies of stem cells and again the techniques to do this did not exist 20 years ago.

Research is a team pursuit and it is wonderful to see the number of principal investigators grow. We now have as clinician scientists, Mr Parwez Hossain studying corneal diseases, Mr Jay Self and Miss Helena Lee studying paediatric diseases and our scientific colleagues Dr Arjuna Ratnayaka and Dr Jörn Lakowski using cell biology to study macular degeneration and retinal cone function. I expect great progress to be made in the next 20 years in terms of our research translating into better treatments for patients and that is really exciting.

Meet Our Team

The current vision science group started with the appointment of Professor Andrew Lotery as Chair of Ophthalmology in 2002.

Since then several principal investigators have been appointed having come through academic training in vision sciences (Jay Self and Helena Lee) while others have been recruited from elsewhere (Parwez Hossain, Arjuna Ratnajaka and Jörn Lakowski). This has led to a diverse group of both clinical and scientific researchers who work together to better understand and treat blinding eye diseases.
A particular strength of the department is the close connection between clinicians and scientists.



Our team is made up of clinicians and scientists from the University of Southampton (UoS) and NHS

1994

The Eye Unit moved from Bedford Place to a purpose-built facility at Southampton General Hospital, at the same time Professor Andrew Elkington launched a fund to raise £1million for research facilities in the unit.

2002

Professor Andrew Lotery was appointed Professor of Ophthalmology.

2004

Gift of Sight, as we now know it, was re-launched.

2007

100+ publications

2010

200+ publications

2013

Dr Arjuna Ratnayaka appointed Lecturer

2014

Dr Jay Self appointed Associate Professor in Ophthalmology

2015

300+ publications

2017

Dr Parwez Hossain awarded The Founders Cup at the 101st Oxford Ophthalmological Congress, for a novel approach to identify micro-organisms involved in corneal infections and provide instant identification of bacteria.

2018

Dr Jörn Lakowski appointed Senior Research Fellow in Visual Science.

Professor Andrew Lotery awarded £4 million Wellcome Trust grant to research the progression of early AMD to late AMD.

2019

Dr Helena Lee appointed Associate Professor in Ophthalmology

2020

400+ publications

2021

Dr Helena Lee awarded £1.4 million by the Medical Research Council (MRC) for her work on the OLIVIA study

2022

Dr Arjuna Ratnayaka Associate Professor

1994 ····· 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022

Meet Our Experts

Andrew Lotery MD, FRCOphth

Professor of Ophthalmology, Honorary Consultant Ophthalmologist, Research Director for Gift of Sight Appeal

Andrew's clinical specialty is medical retina with major research interests in age-related macular degeneration, central serous chorio-retinopathy and inherited retinal diseases.

In 2009 he was awarded the Nettleship Award for best research published by a UK ophthalmologist in the past 4 years by the Royal College of Ophthalmologists and was listed in the Times as one of the United Kingdom's top 100 doctors. His research has been recognised by the University Hospital Southampton Innovation and Researcher of the Year awards in 2012, 2014 and 2017 and a Macular Society award. He was Editor in Chief of the scientific journal, Eye for 10 years. He and his team have performed over 127 clinical trials and published over 400 papers in high impact journals including Nature Genetics, Nature Communications, the Lancet and the New England Journal of Medicine. He has served twice as an NIHR Senior Investigator and raised grant funding totalling over £17 million.

KEY AREAS OF RESEARCH

- Age related macular degeneration - AI, cell biology, clinical trials, genetics.
- Central serous chorioretinopathy - clinical and genetics.
- Stargardt disease.
- Gene therapy for retinal diseases - clinical and laboratory.
- Glaucoma - genetics.

TOP 5 PUBLICATIONS

1. Eplerenone for chronic central serous chorioretinopathy in patients with active, previously untreated disease for more than 4 months (VICI): a randomised, double-blind, placebo-controlled trial. Lancet (2020).
2. Rare Genetic Variants in Complement Factor I Lead to Low FI Plasma Levels Resulting in Increased Risk of Age-Related Macular Degeneration.Invest Ophthalmol Vis Sci (2020).
3. Age-related macular degeneration and modification of systemic complement factor H production through liver transplantation. Ophthalmology (2013).
4. Association between the SERPING1 gene and age-related macular degeneration: a two-stage case-control study. Lancet (2008).
5. A single EFEMP1 mutation associated with both Malattia Leventinese and Doyne honeycomb retinal dystrophy. Nat Genet (1999).

Parwez Hossain MBChB, PhD, FHEA, FRCOphth, FRCS (Ed)

Associate Professor & Clinical Lead for Corneal Services, Consultant Ophthalmic Surgeon

Parwez leads an investigative research programme to improve the health of patients with corneal diseases. His work principally focuses on understanding and improving diagnostics/ therapies of corneal inflammatory disease.

Parwez's group successfully applied new imaging modalities such as anterior segment optical coherence tomography and corneal confocal microscopy to improve the management of patients with corneal infection disease.

Parwez's lab has replicated the immune-kinetics of human bacterial infection, using the human ex vivo whole cornea infection model. This has provided valuable knowledge into the rapidity of gram-negative infection and the impact of antimicrobial therapy. His group were the first to show the real-time morphological and inflammatory parameters that distinguish different types of corneal infection.

Parwez has also, with his University's Engineering colleagues, developed novel platforms for instant pathogen identification for corneal infections and new laser technology for corneal transplantation to improve surgical outcomes.

KEY AREAS OF RESEARCH

- Host-pathogen interactions in microbial keratitis.
- Immunobiology of corneal diseases.
- In-vivo corneal imaging with Spectral-Domain Optical Coherence Tomography.
- Corneal Confocal Microscopy.
- Rapid pathogen identification using novel chip on lab platforms.
- Novel Optimised Laser-Based Platforms for Corneal Transplantation.

TOP 5 PUBLICATIONS

1. Neurotrophic keratopathy, Progressive Retinal and Eye Research (2018).
2. Phase I Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis, Ophthalmology (2018).
3. Lipopolysaccharide regulation of toll-like receptor-4 and matrix metalloprotease-9 in human primary corneal Fibroblasts, Investigative Ophthalmology and Visual Science (2011).
4. In vivo quantification of bacterial keratitis with optical coherence tomography, Investigative Ophthalmology and Visual Science (2011).
5. Early detection of diabetic peripheral neuropathy with corneal confocal microscopy, Lancet (2005).

Jay Self BM, FRCOphth, PhD

Associate Professor & Consultant Ophthalmologist

Jay completed his medical training in Southampton and Manchester and his research training through an MRC Clinical Research Training Fellowship/PhD in Ophthalmic Molecular Genetics.

Jay's research interests cover a range of disorders affecting vision in children with a particular focus on nystagmus, albinism and amblyopia. His team combines expertise in genetics, bioinformatics, wet-lab modelling, eye-tracking, amblyopia research and clinical trials.

Jay is an advisor, board member, grant panel member or ambassador for 7 charities. He is an elected member of the Royal College of Ophthalmologists (RCOphth) paediatric, academic and genomics subcommittees and chair of various national masterclass training courses. He is the NIHR paediatric and neuro-ophthalmology CSG national chair, lead for undergraduate Ophthalmology at UoS and is a keen advocate of public engagement in science.

Jay and his team seek to improve the care for children with visual disorders by advancing diagnostics, developing novel treatments and disseminating best practice.

KEY AREAS OF RESEARCH

- Novel therapeutics for Albinism - drug discovery and lab studies.
- Diagnostics for Albinism and Nystagmus - genetic and genomic studies seeking to improve diagnosis.
- Amblyopia - Clinical trials and harnessing novel technology to aid treatment.
- Clinical electrophysiology - novel diagnostics tools in children.
- Research into support and information for people with nystagmus including PPI work.

TOP 5 PUBLICATIONS

1. Identification of a functionally significant tri-allelic genotype in the Tyrosinase gene (TYR) causing hypomorphic oculocutaneous albinism (OCA1B), Scientific Reports (2017).
2. Mutation of EPT1 (SELENOI) underlies a new disorder of Kennedy pathway phospholipid biosynthesis, Brain (2017).
3. Comparison of mouse and human retinal morphology and function in albinism: potential implications for therapeutic development, The Lancet (2017).
4. Infantile nystagmus and late onset ataxia associated with a CACNA1A mutation in the intracellular loop between s4 and s5 of domain 3, Eye (2009).
5. Allelic variation of the FRMD7 gene incongenital idiopathic nystagmus, Archives of Ophthalmology (2007).

Helena Lee MB, BCh, BAO, PhD, FRCOphth

MRC Clinician Scientist Fellow, Associate Professor in Ophthalmology

Helena specialises in neuro-ophthalmology, paediatrics and strabismus and has an international research reputation in the area of infantile nystagmus, pediatric retinal development and optical coherence tomography (OCT).

She has researched the effects of idiopathic infantile nystagmus, achromatopsia and albinism on retinal development and was awarded the Fight for Sight Award in 2015 for her work on normal retinal development. She has recently been awarded a £1.4 million MRC Clinician Scientist fellowship to investigate the role of Oral Levodopa in improving Visual development in Infants and young children with Albinism (the OLIVIA study). She was awarded the RSM Squint Forum Prize in 2020 for her work on the OLIVIA project.

KEY AREAS OF RESEARCH

- Nystagmus
- Retinal development
- Neuroplasticity
- Optical coherence tomography
- Treatment development for albinism

TOP 5 PUBLICATIONS

1. Management of nystagmus in children: a review of the literature and current practice in UK specialist services, Eye (2020).
2. Oral levodopa rescues retinal morphology and visual function in a murine model of human albinism, Pigment Cell Melanoma Research (2019).
3. In Vivo Foveal Development Using Optical Coherence Tomography, Investigative Ophthalmology and Visual Science (2015).
4. Is handheld optical coherence tomography reliable in infants and young children with and without nystagmus? Investigative Ophthalmology and Visual Science (2013).
5. Potential of handheld optical coherence tomography to determine cause of infantile nystagmus in children by using foveal morphology, Ophthalmology (2013).

J. Arjuna Ratnayaka PhD

Associate Professor in Vision Sciences

Dr Ratnayaka is a Cell Biologist who studies how tissues in the retina becomes diseased with old age.

He also investigates retina-brain links including the mechanisms that underpin neurodegenerative conditions such as Alzheimer's disease. His group utilizes in-vitro cell and mouse models as well as human donor tissues; employing approaches such as the use of induced pluripotent stem cells, gene-editing, lentiviruses and 3D-imaging for their studies. His discoveries have led to collaborative projects with industrial partners. Dr Ratnayaka also investigates the policy implications of his work. He serves in several scientific and academic advisory panels, and acts as a peer-reviewer for UK and international funding organisations. He is also involved in raising awareness of blinding diseases and dementia through public lectures, workshops and outreach activities.

KEY AREAS OF RESEARCH

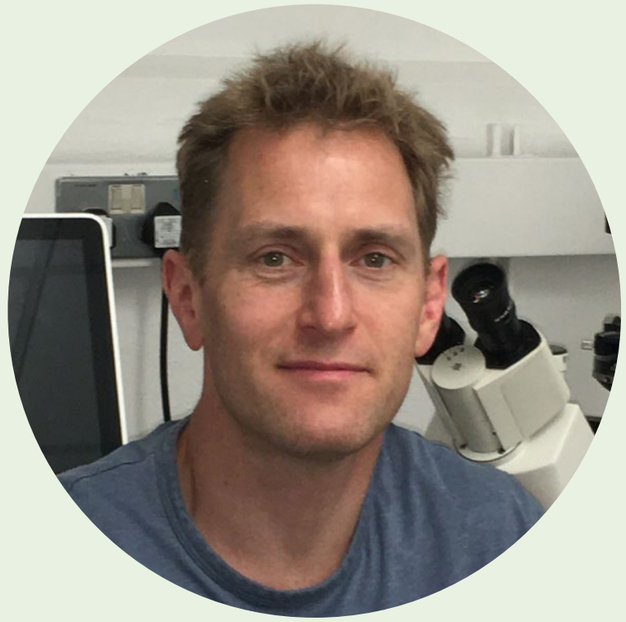
- Retinal cell biology
- Ageing
- Nutrition
- Disease modelling
- Animal models
- Neurodegeneration

TOP 5 PUBLICATIONS

1. Oligomeric Aβ1-42 Induces an AMD-Like Phenotype and Accumulates in Lysosomes to Impair RPE Function. Cells. 2021 Feb 17;10(2):413
2. 3D-Reconstructed Retinal Pigment Epithelial Cells Provide Insights into the Anatomy of the Outer Retina. Int J Mol Sci. (2020).
3. An In-Vitro Cell Model of Intracellular Protein Aggregation Provides Insights into RPE Stress Associated with Retinopathy. Int J Mol Sci. (2020).
4. A lasered mouse model of retinal degeneration displays progressive outer retinal pathology providing insights into early geographic atrophy. Sci Rep. 2019 May 16;9(1):7475.
5. Oxidative Stress and Dysfunctional Intracellular Traffic Linked to an Unhealthy Diet Results in Impaired Cargo Transport in the Retinal Pigment Epithelium (RPE), Molecular Nutrition and Food Research (2019).

Jörn Lakowski PhD

Senior Research Fellow in Vision Sciences



Dr Jörn Lakowski is a Senior Research Fellow in Vision Science within the Faculty of Medicine.

His research focuses on understanding photoreceptor development and disease by utilizing pluripotent stem cells in conjunction with genome engineering tools to develop treatments for inherited retinal diseases. Jörn undertook his graduate studies at the Department of Cellular Biology at University of Georgia (USA), and obtained his PhD in 2007. He developed an interest in utilizing lessons learned from studying developmental biology to establish treatments for retinal diseases such as retinitis pigmentosa and cone dystrophy. For his post-doctoral work, Jörn joined Professor Sowden's team at the Institute of Child Health, University College London, focussing on developing a cell therapy for retinal degeneration. He obtained a Fight for Sight Early Career Investigator Award and established his first independent research group in 2014. In 2018, Jörn moved to the University of Southampton to join the Vision Group.

KEY AREAS OF RESEARCH

- Disease modelling retinitis pigmentosa using hPSC derived retinal organoids
- Drug screening related to treatment of retinitis pigmentosa
- Developmental cell biology of the retina
- Understanding cone photoreceptor migration GPCR signalling in early cone photoreceptor development

TOP 5 PUBLICATIONS

1. Generation of a Cone Photoreceptor-specific GNGT2 Reporter Line in Human Pluripotent Stem Cells, Stem Cells 2022
2. Isolation of human photoreceptor precursors via a cell surface marker panel from stem cell-derived retinal organoids and fetal retinae, Stem Cells (2018).
3. Isolation and Comparative Transcriptome Analysis of Human Fetal and iPSC-Derived Cone Photoreceptor Cells, Stem Cell Reports (2017).
4. Transplantation of photoreceptor precursors isolated via a cell surface biomarker panel from embryonic stem cell-derived self-forming retina, Stem Cells (2015).
5. Photoreceptor precursors derived from three-dimensional embryonic stem cell cultures integrate and mature within adult degenerate retina, Nature Biotechnology (2014).

Meet Our Clinical Team

Magdalena Ansari

Senior Research Ophthalmic Photographer

"I completed my degree in Poland as Orthoptist and Ophthalmic Technician, moving to the UK to improve my career opportunities. I started working at Southampton Eye Unit fifteen years ago, in 2006, and am happy to be a part of the research team. As a Senior Ophthalmic Photographer my responsibilities are both clinical and research focused, this has developed and maintains a tremendous practical knowledge skillset. This is required for the very sophisticated equipment that we have at Southampton Eye Unit.

One of the proudest moments was when I was the first person in the UK to lead and train an imaging team and doctors to do qAF and Adaptive Optics.

I am proud to work in one of the UK's major teaching hospital, and it is a joy to apply my knowledge into practice with patients whilst doing research."

Samir Khandhadia

Speciality Dr in Ophthalmology

"I started working at Southampton Eye Unit in 1999 as a full time clinician specialising in Medical Retina and Research. Since then I have completed a PhD that was supervised by Professor Lotery. The focus of my PhD was on genetics, age-related macular degeneration, and association with liver transplantation - investigating whether changing production of a particular protein can affect AMD. I am still involved in many research projects as my position has continued to develop."

Thea Sass

Senior Research Sister

"I started as an Ophthalmology Research Nurse January 2014. I previously worked in the Eye Unit at Hampshire Hospitals Winchester and always had a keen interest in clinical research. In my role as Research Nurse I was involved in all stages of research delivery including managing a portfolio of studies. In my current role as Senior Research Sister I continue to have oversight of the Ophthalmology team – setting up studies, liaising with commercial and non-commercial sponsors and supporting the team to deliver high quality research and care to our research participants."

Mohamed ElDakkak

Speciality Doctor in Medical Retina

"I started a long journey in the field of medical retina and uveitis as a fellow, then a consultant in the leading eye hospital in the Middle East (MAGRABI Hospitals) from 2011 to 2019 in KSA after a medical graduation and an Ophthalmology residency training in Egypt back to 2005 with a master degree in Ophthalmology in 2009. During this journey, I also had my FRCS degree from Glasgow, UK in 2012 and my Uveitis training in New York Eye and Ear Infirmary, USA in 2015 and I was also attending many local and international conferences as a presenter and an instructor. This all helped me to build up an extensive experience in this field as being exposed to variable and different challenging cases around the world."

Our PhD students

Rebecca Miller

PhD Candidate

I am in the second year of my PhD focusing on dry Age-related Macular Degeneration (AMD) within the Vision Group. I previously studied Biomedical Science with a focus on Physiology and Pharmacology at Leeds Beckett University, followed by a Master's degree in Molecular Neuroscience at the University of Bristol.

After studying, I worked at the University of Oxford gaining practical experience in clinical research and lab management. As I was applying for PhDs, this project stood out in particular as it had a mix of familiar techniques I was very proficient at, such as cell culture and imaging, as well as unfamiliar methods such as confocal microscopy and transient transfections. The project was additionally appealing as one of the main aims is to develop a viral construct which could be used as a novel therapy to treat AMD, which currently has no cure.

My goals for the future would be to continue in academic research, and hopefully start my own research group one day.

20 YEARS OF VISION SCIENCES

Our PhD Students

DATE	NAME	SUPERVISOR	CO-SUPERVISOR
Current	Anna Muir	Arjuna Ratnayaka	Andrew Lotery, Helena Lee
Current	Charles Ellis	Arjuna Ratnayaka	Louise Serpell (University of Sussex)
Current	Stephanie Turner	Arjuna Ratnayaka	Andrew Lotery, David Tumbarello
Current	Catherine Robertson	Jorn Lakowski	Andrew Lotery
Current	Rebecca Kaye	Andrew Lotery	Jorn Lakowski
Current	Sarah MacDonald	Helena Lee	Arjuna Ratnayaka, Jay Self
Current	Rebecca Miller	Arjuna Ratnayaka	Andrew Lotery, David Tumbarello
2019	Luke O'Gorman	Sarah Ennis	Andrew Lotery, Jay Self
2019	Chelsea Norman	Jay Self	Arjuna Ratnayaka, Diana Baralle
2019	Charlotte Collier	David Tumbarello	Arjuna Ratnayaka
2019	Ahmed Salman	Jay Self	Andrew Lotery
2019	Ilaria D'Atri	Andrew Crosby	Emma Baple, Jay Self
2018	Eloise Keeling	Arjuna Ratnayaka	Andrew Lotery, David Tumbarello
2017	Savannah Lynn	Arjuna Ratnayaka	Andrew Lotery, Tracey Newman and Angela Cree
2016	Gareth Ward	Martin Grossel	Andrew Lotery, Arjuna Ratnayaka
2016	Thomas Hallam	David Kavanagh	Andrew Lotery
2016	Ahmad Elsahn	Parwez Hossain	Myron Christodoulides
2016	Konstantopoulos Aristides	Parwez Hossain	Myron, Christodoulides
2013	Sam Khandhadia	Andrew Lotery	Parwez Hossain
2012	Xiaoli Chen	Andrew Lotery	Parwez Hossain
2009	James Self	Andrew Lotery	Andrew Collins
2008	Srinivas Goverdhan	Andrew Lotery	Martin Howell
2007	Neda Bogari	Andrew Lotery	

Academic Training in Ophthalmology

NIHR Academic Clinical Fellowship in Ophthalmology, University of Southampton, UK.

The NIHR academic clinical fellowship provides protected time for junior ophthalmologists to undertake research at the University of Southampton. During their first three years of training as ophthalmologists they spend 9 months working in the Vision Science laboratories in Southampton on their specific project with the aim of obtaining preliminary data to fund a PhD prior to them progressing to a lectureship and subsequent independent research career. These fellowships are awarded in a national competitive process and Southampton has been successful every time an application has been applied for. Dr Rebecca Kaye was a recent academic fellow and is now undertaking her PhD funded by the Wellcome Trust. Rebecca is studying under the supervision of Professor Lotery and Dr Jörn Lakowski the function of a gene implicated in the development of age related macular degeneration. This involves learning novel techniques including stem cell culture and CRISP-CAS9 genome editing.

Adnan Khan
BSc MB BS PhD FRCOphth

NIHR Clinical Lecturer in Ophthalmology, University of Southampton

The University of Southampton is one of the few UK research universities to offer a formal clinician-scientist training route in ophthalmology. National Institute of Health Research (NIHR)-funded academic ophthalmology posts have been awarded to the University due to the research strengths of the Vision Sciences Group under the mentorship of Professor Andrew Lotery. Medical doctors in ophthalmology can combine their formal clinical training with protected pre- and post-doctoral (post-PhD) research time.

I joined the Vision Sciences Group to undertake post-doctoral research in ocular immunology under Professor Lotery's guidance, and complete my higher specialty training in ophthalmic surgery at Southampton Eye Unit. My current research explores the inflammatory mechanisms underlying Age-Related Macular Degeneration (AMD). In particular, I am running a clinical study together with Professor Lotery investigating the effect of an ageing immune system on the progression of AMD. This builds upon my previous clinician-scientist training posts in London and Oxford, and complements my clinical sub-specialties of uveitis (intraocular inflammation) and medical retina.

COVID-19 Response Impact on Eye Research

Tracey Jones is a Ophthalmology Research Nurse based in the Eye Unit at Southampton General Hospital

We have all stepped up to play our part since the start of the pandemic, but little did I know when I joined the Eye Research Team in December 2019 from Eye Outpatients Department (OPD) that I would be working on Inpatient COVID studies only a few months later. Many of the Eye OPD team went to work in the Emergency Department or wards, and the usually busy clinics quickly became mask wearing, socially distanced, reduced numbers environments, or virtual clinics.

New research studies were put on hold, and nearly two years later we are still working through the catch-up period.

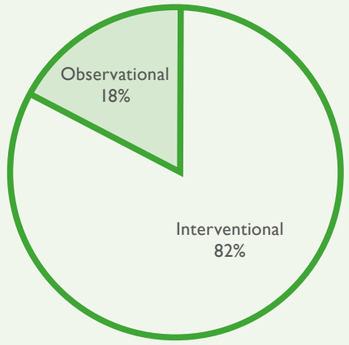
Most of the Eye Research team helped on COVID studies, but I was seconded for a year helping to run RECOVERY an international study looking at potential COVID treatments, some of which became standard care, others proven to not be effective. I also helped with recruitment, data entry, and sample collection for several other COVID studies.
I saw patients who were frightened and struggling to breath, distressed at not being able to see their families, many going to the Intensive Care Unit for weeks or months – some never recovering. It was so humbling that patients who were very unwell, several of whom had also lost relatives to COVID, wanted to take part in the studies to help others, even if it would not help them.

> "There were so many positive things that came out of my time working in research during the pandemic"

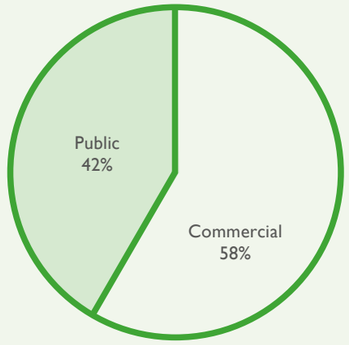
Despite the challenges of working in a completely new environment and speciality, as well as the emotional toll, there were so many positive things that came out of my time working in research during the pandemic – getting to know, and working as part of, an amazing team who were always there for each other, providing great support when times were tough; the opportunity to learn about 'all things respiratory'; helping to make a difference to the patients we came into contact with; and working on studies to help find COVID treatments has given me a sense of pride at being part of the bigger picture.

Past Research

One of our key goals is to publish our research so that it is of benefit to the wider scientific community.



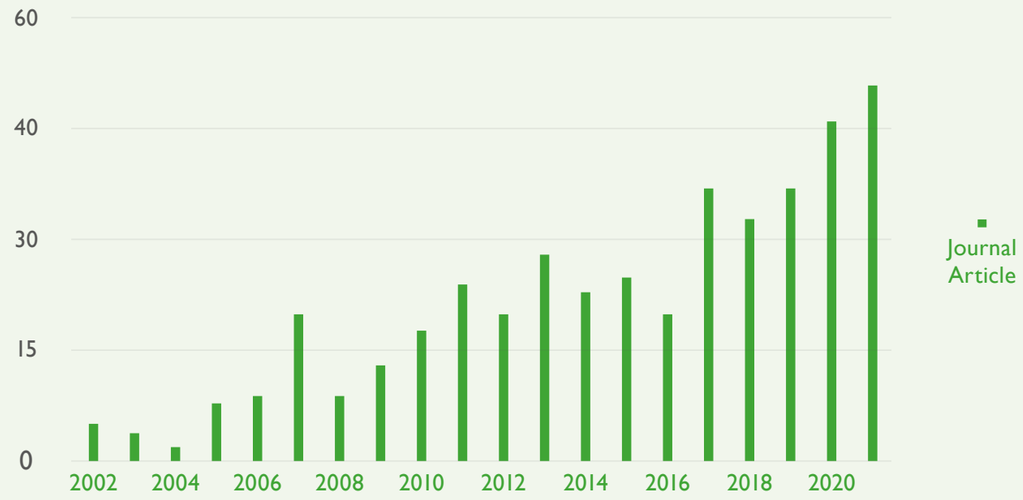
Types of Research

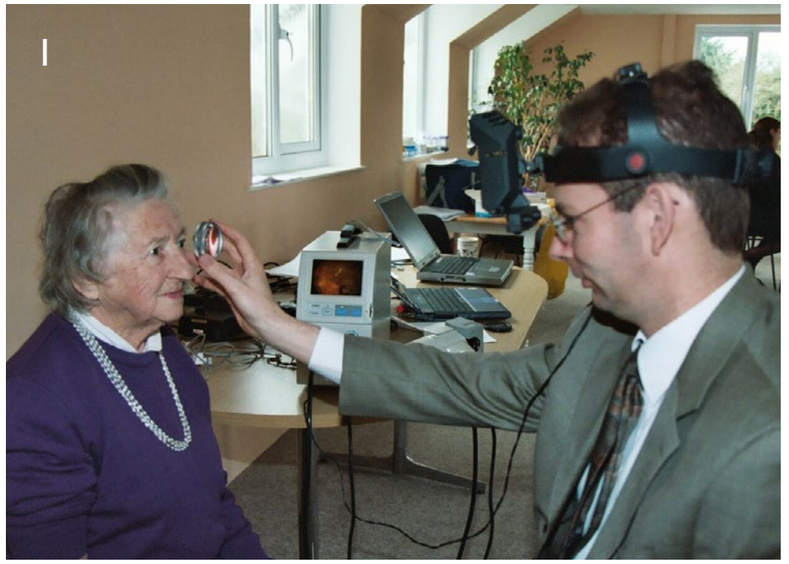


Funding: Commercial v Public 2012-2021

These charts show how our research productivity has grown year on year with increasing numbers of publications. Our research was also chosen for an impact case study in the UK government's 2021 research assessment of UK universities research productivity and was ranked in the top 10 % of all such case studies. As these pie charts show our research is mostly interventional which is in line with what our patients want i.e. novel treatments. Our funding is balanced between public and commercial funding as we work with commercial bodies to translate new drug treatments into the clinic and public funding bodies to support our more basic science research.

Publications by Vision Sciences 2002 - 2021





PAST RESEARCH IMAGES

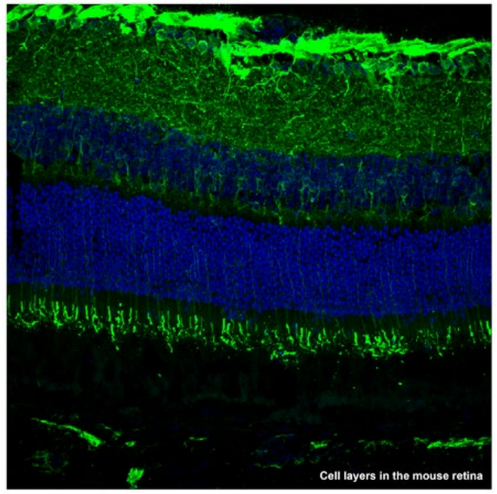
1. Professor Lotery examing a patient on a field trip to Guernsey in 2003.
2. PhD student Mr Goverdhan takes a blood sample from a volunteer in Guernsey.
3. The Guernsey Blind Association kindly provided space for our research trips.
4. Research technician Kim Avery takes a medical history from a volunteer in Guernsey.

Current Research Studies

Mouse models of age-related macular degeneration (AMD)

DR ARJUNA RATNAYAKA

Title of Study	Mouse models of age-related macular degeneration (AMD)
Chief Investigator	Dr Arjuna Ratnayaka
Funders	National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3R), Macular Society, Fight for Sight, Alzheimer's Research UK, Sight Research UK and the Gift of Sight Appeal
Combined awards	£310,195
Research Organisation	University of Southampton
Co-investigators	Professor Andrew Lotery, Dr Helena Lee, Dr Tracey Newman, Dr Felino Cagampang and Professor Jessica Teeling


Cell layers in the mouse retina

WHY IS THE RESEARCH NEEDED?

Blinding conditions such as age-related macular degeneration (AMD) are caused by a combination of disease-linked genes, lifestyle risk factors including an unhealthy diet and smoking, as well as ageing. These come together to bring about disease in the retina, which are both complex and difficult to study. To help understand how AMD initially develops and progresses to cause blindness, researches have turned to animal models, most commonly rodents. Mice allow scientists to assess how particular AMD risk genes can trigger retinal degeneration. It is also possible to test the effects of lifestyle risks and combine these with the effects of ageing. Mouse models that develop AMD-like features are therefore important tools, allowing specific disease-causing pathways and their combinations to be teased-out and studied in a manner not possible by other means. In the past, a mouse model where the growth of new blood vessels under the retina could be triggered was used to develop anti-VEGF treatments, which is now the main therapy for wet AMD patients. These AMD-like mouse models are therefore of critical importance and could help develop effective future treatments. Lack of suitable animal models to test new drugs often coincides with either ineffective or no treatment at all. For instance, there are no suitable mouse models with dry AMD-like features; a condition which currently also has no cure.

WHAT ARE THE STUDY FINDINGS?

To address this important knowledge gap, researchers at Southampton set out to develop new mouse models which develop important AMD-like features. Over the course of 8 years and competitively funded by PhD studentships and project awards from multiple funding organisations, we developed and published details of three mouse models with AMD-like features. Importantly, retinal pathology in these models are triggered by different AMD risk factors, reflecting the multifactorial causes of this complex disease. The first of these models, which used a laser, reproduced a central retinal lesion and showed evidence of degeneration, as reported in dry AMD patients. The second model was generated by exposing mouse retinas to the Alzheimer's-associated amyloid beta (Aβ) proteins. These toxic proteins also collect in human retinas with age and are found at high levels in retinas of AMD patients. Mouse retinas exposed to Aβ also developed a central retinal lesion. In the third mouse model, we showed that consuming an unhealthy "Western-style" diet resulted in developing early-intermediate features of AMD, including subretinal drusen (protein/lipid deposits under the retina), which is the first clinical indicator of AMD in patients.

HOW WILL OUR DISCOVERIES ADVANCE KNOWLEDGE TO BENEFIT PATIENTS?

Our findings have uncovered how different disease-causing pathways singly and in combination can result in retinal damage, thus providing new insights into the causes of AMD. Developing mouse models with dry AMD-like features is of significant value. A fourth mouse model with AMD-like features is currently in development. Our work has attracted interests from other scientists and clinicians, but also from pharmaceuticals companies, where we are collaborating to develop effective new treatments for future AMD patients.


Dr Savannah Lynn


Dr Ellie Keeling

Current Research Studies

Preventing cone starvation in retinitis pigmentosa

DR JÖRN LAKOWSKI

Title of Study	Preventing cone starvation in retinitis pigmentosa
Chief Investigator	Dr Jörn Lakowski
Funder	Academy of Medical Sciences
Award	£118,000
Sponsor	University of Southampton

AN UNMET CLINICAL NEED.

Retinitis pigmentosa (RP) is a major cause of blindness worldwide with a prevalence of 1:4000. With over 80 disease-causing genes identified, RP is the most common type of inherited retinal degeneration. It is characterized by an initial loss of night vision as a result of the malfunction and death of rod photoreceptors. This early phase is followed by a loss of cone photoreceptors. Because cones are required for high-acuity and colour vision, their loss leads to a severe reduction in the quality of life as patients experience reduced autonomy, social isolation and challenges with activities of daily living.

Research has shown that cones depend on rods for a chemical survival signal, termed the "rod derived cone viability factor", which allows the cones to take up the necessary nutrients from their environment. As rods are lost during the course of the disease so is this signal, resulting in "starvation" and eventual loss of cones over time.

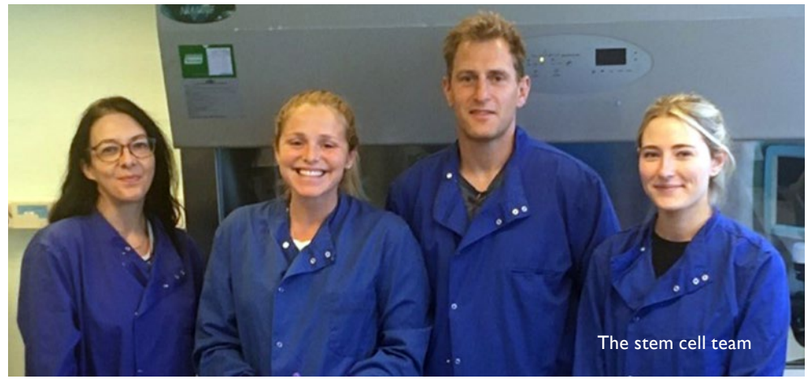
Unfortunately, this process is irreversible and there are no effective treatments available.

WHAT IS THIS PROJECT TRYING TO ACHIEVE?

Supported with a grant from the Academy of Medical Sciences this project aims to reveal the molecular machinery that triggers the death of cone photoreceptors in retinitis pigmentosa. Equipped with this knowledge we would then be able to devise methods to artificially replace the cone survival signal in the form of drugs.

HOW IS THIS RESEARCH CONDUCTED?

Obtaining rods and cones from patients suffering from RP is not possible. Instead, we have developed methods to grow "retinal organoids" or mini-retinas, using human stem cells in our laboratory. Employing the latest genome engineering technology, we have modified these mini-retinas in a way that now mimics the starvation of cones as experienced in RP. In addition, we have engineered the cones to emit a red fluorescent signal that allows us to visualize, track and isolate them for a range of applications. Using this system, we will grow in the lab large numbers of cones, expose them to stringent starvation conditions as seen in RP, and at the same time treat the cells with a chemical library, containing approximately 2000 clinically approved drugs. Those drugs found to mimic the cone survival signal and prevent cone death will be would form the basis of a future drug therapy for retinitis pigmentosa. The use of such repurposed drugs would significantly shorten the time that is required for clinical trials and translation into the clinical setting, as they are considered safe.



The stem cell team

Image on page 24 – Retina in a dish: cones grown within a retinal organoid from embryonic stem cells. Red: fluorescent cone specific reporter, green OPN1LW antibody staining.

Current Research Studies

The OLIVIA Study

DR HELENA LEE

Title of Study	The OLIVIA Study
Chief Investigator	Dr Helena Lee
Funder	Medical Research Council
Award	£1.4 million
Sponsor	University of Southampton
Collaborators	

WHY?

Currently there are no treatments for the eye problems caused by albinism. The average vision in albinism at, 20/80, is below UK driving standards, impacting school, work, and social life. Finding a treatment that can improve eyesight in albinism was named a priority by the Sight Loss and Vision Priority Setting Partnership in 2013.

WHAT WE KNOW ALREADY

We know that the brain has the amazing ability to change and adapt in children. We also know that we make use of the brain's ability to rewire itself, when we improve eyesight in lazy eyes using glasses and patching. In albinism, a chemical called L-DOPA is missing from the eye and this causes problems with eye development. This is why eyesight is so poor in albinism. However the eye is still able to change and develop in young children with albinism. Similar to the treatment of lazy eyes we can target this flexibility in albinism. Potentially, replacing L-DOPA in albinism at a young age, will improve eye development and eyesight.

AIMS OF THE STUDY

The main aim of this study is to prove for the first time that we can change how the eye develops and improve eyesight in albinism after birth, by replacing the missing L-DOPA. We will also figure out what the best dose of L-DOPA is, by testing its effects on eye development and eyesight in mice with albinism, when given at different ages, doses and lengths of time.

The second aim of this study is to carry out a small trial of L-DOPA treatment in children with albinism.

L-DOPA is a safe medicine that is currently being used to treat infants and young children born with problems in controlling movement of their limbs. We will explore, together with the parents of the affected children, if the treatment and examinations carried out as part of this trial are reasonable. If successful, this study will completely change how children with albinism are treated. It will also set an important precedent for the development of new treatments for other eye diseases that affect children.

THE BENEFITS

The biggest potential beneficiaries of this research will be the infants and young children with albinism, his/her family and society at large. It will provide valuable guidance on the optimal treatment interval, the risk of complications, tolerance and uptake of the treatment. It will also employ outcome measures that are useful for service-users and health policy makers and establish the acceptability of this intervention to service users.

This research will also help to streamline and accelerate research into albinism and other disorders of retinal development, through the creation of a freely available on-line repository of murine retinal optical coherence tomography (OCT) imaging and electroretinography data, and a detailed human albinism genotyping and phenotyping database.

Our approach towards developing an effective treatment for albinism serves as an excellent example of how clinical observations at bedside can be taken back into the laboratory for more detailed mechanistic investigations and novel therapeutics development which can then be translated back into clinical practice.

Current Research Studies

The PINNACLE Study

PROFESSOR ANDREW LOTERY

Title of Study	The PINNACLE Study
Chief Investigator	Professor Andrew Lotery
Funder	The Wellcome Trust
Award	£4.3 million
Sponsor	University of Southampton
Collaborators	4 international, 4 UK-based

WHY IS THE RESEARCH NEEDED?

Age-Related Macular Degeneration is the commonest cause of blindness in the elderly. By 2020, 200 million people are expected to be affected, increasing to nearly 300 million by 2040. Unfortunately, doctors don't know who will progress to the sight threatening stage of the disease. Some patients progress slowly or not at all and others quickly. From this study we aim to be able to predict an individual's disease outcome and therefore tailor their treatment pathway to ensure early intervention and the best possible outcome.

WHO IS INVOLVED?

The PINNACLE study is funded by a £3.9 million NIHR Collaborative grant that was awarded to Professor Lotery in 2018. It's a 6-year study that uses machine learning of retrospective patient imaging to identify disease progression in AMD. This will then be validated using a prospective study that follows patients for at least 2 years.

HOW ARE WE CONDUCTING THE RESEARCH?

We can teach computers to analyse high resolution images of the inside of the eye. From UK Biobank and local eye clinics, we have access to hundreds of thousands of such images from people with AMD as well as those without.

These images will allow us to train computers to identify what eye changes appear in patients with AMD. Alongside these images we also have access to DNA results that we can match up to the images to see whether specific DNA changes affect the progression of AMD in individuals.

To validate the AI findings, a study is being run alongside that involves the recruitment of 400 participants for images to be taken every 4 months for at least two years. If changes are identified they will receive additional imaging at the site of the changes.

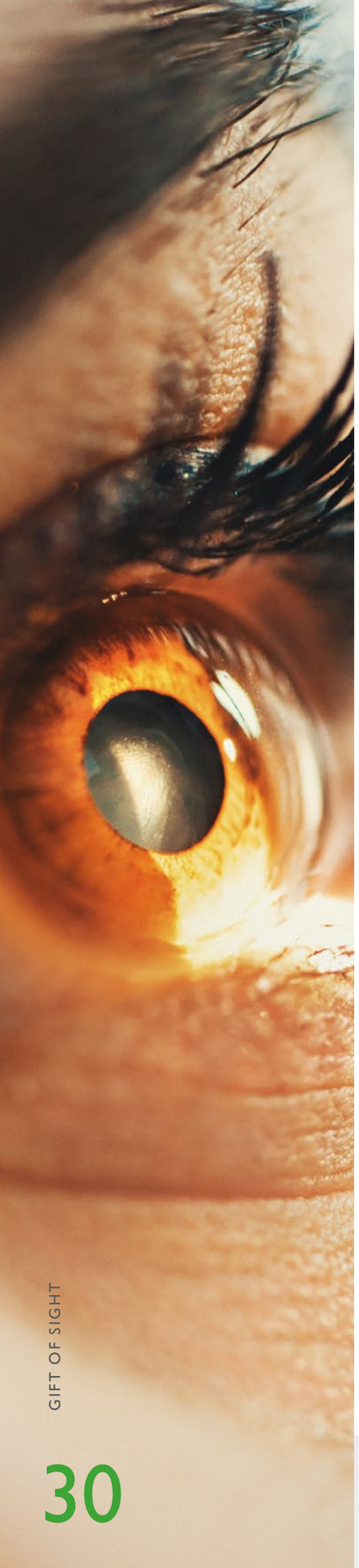
WHAT WILL BE THE OUTCOMES?

A better understanding of AMD progression resulting in a predictive model of AMD progression that can be tailored to individuals at diagnosis. This will allow treatment to be given as early as possible.

Ms Angela Cree

Ms Helen Griffiths

Ms Janice Sutton



Impact with Patients

SORSBY FUNDUS DYSTROPHY PATIENTS: CLAIRE STREET AND EMMA ROACH

We are sisters and both have Sorsby Fundus Dystrophy (SFD). Our Dad lost his central vision within twelve months of noticing the first symptoms and, at the time of his diagnosis in 1990, there was no treatment available for this disease.

Claire was diagnosed with SFD in 2006, although by the time of her referral she had lost much of her central vision in one eye. In 2007 Professor Lotery organised genetic testing in Southampton for the family and, when Emma's vision started worsening in 2012, her treatment was able to start quickly.

We both attend Southampton Eye Unit on a regular basis to keep our vision stable. Neither of us can drive so we rely on our mum to take us to and from appointments. We can both see images on television, walk during the day and can read using a screen but the 'down side' is that we are unable to drive and find it hard to read letters and bills with small writing. Thankfully computer technology, visual aids and requesting help from our families helps us cope.

Our family were delighted to donate skin samples for use by scientists in Southampton, which allows different types of laboratory experiments to be undertaken than could be made with just blood samples.

We both hope that a less invasive type of treatment may be available in the future but are thankful for the care and commitment we experience from the clinical team in Southampton Eye Unit. Our family avidly follow scientific research, were delighted to see our cells in the laboratory and are great supporters of, and advocates for, Gift of Sight.

CLAIRE & EMMA

Gift of Sight

Sight loss costs the UK economy over £28 billion each year but only 1% of public grant funding for medical research is spent on eye research, which is just £20 for each person living with sight loss.

The University of Southampton gift of Sight Appeal was set up in 2004 to help support vision science researchers, led by Professor Andrew Lotery. Whilst grant income is an essential part of academic life, there are times when this does not cover all the costs involved with running a growing team. Philanthropic donations to Gift of Sight have helped purchase Items such as imaging equipment, laboratory freezers and incubators and have supported salaries for technicians, post-doctoral scientists and PhD students.

During the five years from August 2016 – July 2021 Gift of Sight income amounted to £3,094,600.16, with the largest gifts being received from legacy donors, usually patients who have been grateful for treatment received and who wish to help researchers develop new treatments for people who suffer with eye disease in the future. As well as legacy gifts other income streams include regular direct debit income, fundraising events held by generous supporters, events such as an annual Christmas Concert held in Romsey Abbey, gifts sent in memory of friends and relatives who have died and one-off donations.

If you would like to donate to Gift of Sight or learn more of its work please contact us via

www.giftofsight.org.uk
Email : info@giftofsight.org.uk
Tel: +44 (0) 23 8059 9073

Events

Bi-Annual Public Lectures

Annual Carol Concert

Frequent Fundraising Events include sponsored runs, skydives, treks, etc.

Our collaborators

Our research is collaborative because by working with the best scientists and doctors around the world we get the best results. These data show our international reach.

LOCATIONS OF OUR COLLABORATORS	
Australia	1
EU	7
India	1
UK	54
USA	5

University of Southampton