

CET 2024 Research Day Abstracts

CORNEAL & CATARACT

**Madhavan
Rajan**

Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

The clinical impact of 'Bench to Bedside' research in corneal disorders

There are several diagnostic, therapeutic and surgical challenges in managing patients with corneal disorders. The gap in knowledge in these areas offers the potential to explore newer ways of improving clinical care to our patients with often sight threatening conditions. In a series of laboratory-based research projects between 2010-2024, we have conducted various studies focusing on A. Improving microbial detection in infective keratitis (iCAM trial), B. Developing corneal drug delivery strategies (In vitro human model), C. Innovative approaches to corneal transplantation (Microthin DSAEK) and D. Cell therapy potential to restore vision in corneal blindness (Exvivo cultured corneal endothelial cells). Each of these projects had their original ideas explored and investigated in our labs in Cambridge before proceeding to clinical trials. In this presentation, I shall briefly present the gap in knowledge that led to these research ideas and their clinical implications in improving the care for patients with severe corneal disorders such as infective keratitis, severe bullous keratopathy and Fuchs dystrophy.

**EMERGENCY
EYE CARE**

Jen Lim

Co-Authors:
Louise Allen
Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

Implementation of the Eye+dot online triage tool in optometry practices

Background:

Much community triage of patients with ophthalmic symptoms is done by optometry practices who do this unremunerated work alongside scheduled appointments. There are thus considerable benefits to an automated triage tool that supports optometrists in efficiently signposting patient to appropriate services.

Study aims:

To evaluate the effectiveness of the eye+dot online tool in supporting triage at optometry practices and assess its accuracy in triaging patients with appropriate urgency.

Methods:

Patients presenting to seven practices with new-onset ophthalmic symptoms were asked to complete eye+dot's conditional branching questionnaire about symptoms and history, with an automated triage disposition being generated based on their responses. Optometrists made their own triage decisions based on eye+dot's symptom report and any additional information requested from patients. Optometrist and eye+dot triage dispositions were compared against a consultant ophthalmologist's retrospective classification of symptoms into risk categories.

Results:

212 patients completed the questionnaire and were triaged by optometrists, with 52 (24.5%) being categorised by an ophthalmologist as high-risk and thus appropriate for urgent review within 24 hours. Eye+dot accurately assigned 45 (87% of) patients with high-risk symptoms to ED/hospital/MECs within 24 hours and all within 48 hours. Eye+dot was not significantly different from optometry triage in sensitivity (86.5% vs 69.2%, $P=0.052$) and significantly superior in specificity (86.2% vs 56.0%, $P=0.0001$). User feedback from patients was highly positive.

Conclusion:

Our study demonstrated the effectiveness of eye+dot at triaging patients in a primary care setting and the potential benefits this can offer to optometrists, patients, and the wider healthcare service.

EMERGENCY EYE CARE

**Anastasia
Mirza-Davies**

Co-Authors:
Fengyi Liu*
School of
Clinical
Medicine,
University of
Cambridge.
Louise Allen,
Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

* = Joint first
author
Ian Tapply
(Cambridge
University
Hospitals)
Tabassom
Sedighi (Vision &
Eye Research
Institute, Anglia
Ruskin
University)
Jost B Jonas.
University of
Heidelberg
Robert Casson.
University of
Adelaide
David Friedman,
Harvard
University
Nicolas Leveziel.
University of
Poitiers
Hugh R. Taylor.
University of
Melbourne

Evaluation of the eye+dot triage tool in the Emergency Eye clinic (EEC)

Background:

High NHS emergency eyecare demand contrasts with the low acuity of many visits. Eye+dot is an online triage tool that uses branching-logic questions to compile a downloadable ophthalmic history report and suggests an appropriate urgency and provider disposition. It may offer a novel approach to reducing pressure on emergency eyecare services.

Methods:

Patients aged 13+ attending Addenbrooke's EEC received eye+dot SMS links. Eye+dot and nursing triage disposition were recorded and an acuity score based on EEC diagnosis was assigned by a consultant ophthalmologist. Specificity and sensitivity to high acuity assignment and inter-rater agreement were calculated for both eye+dot and triage nurse.

Results:

352 eye+dot links were sent. 209 (59%) were completed in an average 5.71 mins (SD +/- 2.59). The mean age of respondents was 47.9(SD +/- 18.7). Eye+dot recommended hospital/community urgent eye service in 186 (89%) of cases. Compared with 'gold-standard' acuity rating, eye+dot showed higher sensitivity (94.30%) and specificity (62%) than EEC triage disposition (82.90% $p = 0.29$; 24.71% $p < 0.001$), as well as better inter-grader agreement (Cohen's Kappa: 0.33 $p < 0.001$ vs. 0.0312 $p = 0.30$). 202 (97%) patients completed Likert score feedback: 165 (82%) rated the test good or excellent, 4 (2%) patients rated the test poor.

Conclusions:

Eye+dot shows promise as an efficient, and acceptable triage support tool. Its automated disposition had a higher accuracy for identifying high acuity diagnoses than the current triage pathway. A large-scale community implementation study is required to understand the effect its use may have on EEC demand.

GLAUCOMA

Vesela
Valchova

Co-Author:
Stylianios
Georgoulas
Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

I Stent inject trabecular micro-bypass combined with cataract surgery reduced Intraocular Pressure and stabilized Visual Fields in glaucoma patients at Cambridge University Hospital

Introduction:

Microinvasive glaucoma surgery has increased the treatment options for glaucoma patients over the last decade. iStent inject W (Glaukos), a recently approved device at Cambridge University Hospital, is designed to lower intraocular pressure (IOP) by creating a bypass through the trabecular meshwork to the Schlemm's canal.

Methods:

Combined phacoemulsification with intraocular lens implant (IOL) plus iStent inject W was performed on 26 eyes of 25 patients from December 2022 until January 2024 at CUH. Retrospective analysis was focused on the effect of this procedure on IOP, number of glaucoma drops, visual field changes, as well as intraoperative and postoperative complications.

Results:

Patients' mean age at the time of surgery was 79.8 years old. Pre-operative IOP was 16.5mmHg (SD \pm 4.5). Post-op IOP at week 1 was 13.9mmHg (SD \pm 4.6, n=23, p=0.06), at month 1, 14.9mmHg (SD \pm 5.5, p=0.136, n=26), at around 6 months 12.6mmHg (SD \pm 3.2, p=0.0005, n=24) and at around 12 months 14.2mmHg (SD \pm 2.3, p=0.0006, n=10). Humphrey 24-2 Sita-Standard MD pre-op was -9.76 dB (SD \pm 6.4). MD at around 4.5 months post-op was -8.9 dB (SD \pm 7 dB, p=0.402, n=24) and at around 9.5 months post-op was -8.12 dB (SD \pm 7.8 dB, p=0.07, n=12). No intra-op complications were encountered in our patients. Two eyes developed post-op cystoid macular oedema, which resolved. One patient underwent additional glaucoma surgery (trabeculectomy) 13 months post op.

Conclusion:

In our cohort of patients, iStent inject W combined with cataract surgery demonstrated safety and effectiveness in lowering the IOP post-operatively and stabilizing visual fields.

GLAUCOMA

**Vesela
Valchova**

Co-Author:
Stylianos
Georogulas
Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

The European Glaucoma Society (EGS) Patients Involvement Initiative - patients' perception of glaucoma care.

Purpose:

There is often low adherence to disease management in glaucoma, as with other chronic diseases, which may arise from shortcomings in care provision. The EGS initiated a patient involvement initiative to identify patient needs so that these may be addressed to improve glaucoma care.

Methods:

Glaucoma patients across Europe were given access to an electronic survey, available in ten languages, between December 2022 and June 2023, consisting of 23.

Results:

We received 3002 responses from 26 European countries. 1849 (61.6%) were female. 1903 patients (63.4%) were between 60-79 years of age and 1804 (60.8%) responders had received higher education. 2776 (93%) had been diagnosed with glaucoma and the rest with ocular hypertension. Although 2167/2774 (78.1%) of the responders were satisfied with their knowledge of glaucoma, 817/2167 (42 %) commented that information about glaucoma had to be sourced by themselves. 2133/2762 (77.1%) of responders stated that they were satisfied with the glaucoma care received in their country. 835/1990 (40.3%) of responders claimed to have had a psychological impact from receiving a glaucoma diagnosis. The top two challenges faced by glaucoma patients were struggling with remembering to apply drops (394/1912, 20.6%), and side effects from drops/medication (261/1912, 13.7%).

Conclusion:

Key knowledge gained from this questionnaire is that patients, in many parts of Europe, are often not given fully comprehensive explanations about their condition and they have to source information about glaucoma by themselves. The EGS will continue its collaboration with patients to better integrate patients' needs into daily glaucoma management.

GLAUCOMA

Nikhil Jain

Co-Authors:

Arun

Thirunavukarasu

. Oxford

University

Academic

graduate School

Rohan

Sanghera.

University of

Cambridge

school of

medicine

Federico

Lattuada .

Department of

Engineering,

University of

Cambridge

Shathar

Mahmood.

University of

Cambridge

School of clinical

medicine

Anna

Economou.

University of

Cambridge

School of clinical

medicine

Helmut Yu.

University of

New South

Wales.

A fully accurate web-based application for automatic classification of glaucomatous visual field defects using Hodapp-Parrish-Anderson criteria.

Purpose:

To evaluate a novel web-based application for grading 24-2 Humphrey visual field test results in accordance with Hodapp-Parrish-Anderson (HPA) criteria.

Methods:

The Glaucoma Field Defect Classifier (GFDC) was designed and deployed online for researchers to utilise (<https://gfdc.app>). 168 consecutively recorded visual fields of 89 glaucoma patients attending clinic at a tertiary referral centre were studied. Each visual field was evaluated by two independent researchers and disagreement resolved by a third researcher acting as arbiter; all using printed HPA criteria to make their appraisals. The same fields were inputted into GFDC and outcomes were compared against gold-standard human assessment to gauge accuracy.

Results:

For every single perimetry result, GFDC produced output which matched human grading based on HPA criteria. The accuracy of GFDC was therefore 100% for each level of visual field grading (mild, moderate, severe). Sensitivity and specificity were also 100%. Interpretability analysis confirmed the web-application correctly identified test loci on perimetry result charts and classified defects based on result legends.

Conclusions:

GFDC, a web-application, exhibits equivalent performance to human graders classifying glaucomatous visual field defects based on HPA criteria. GFDC can facilitate visual field assessment at scale with potential to augment clinical practice and research where application of explicit perimetry criteria is often precluded by time constraints. The code used to build GFDC is freely available online for others to adapt to support use with alternative visual field result formats.

**INHERITED
RETINAL
DISEASE**

Nisha Nixon

Co-Authors:
Kelly Cheng.
University of
Cambridge
Allan Richards.
John van Geest
Centre for Brain
Repair,
Cambridge
Howard Martin.
John van Geest
Centre for Brain
Repair,
Cambridge
Martin Snead.
University of
Cambridge,
John van Geest
Centre for Brain
Repair,
Cambridge,
Cambridge
University
Hospitals NHS
Foundation Trust
Brinda
Muthusamy.
Cambridge
University
Hospitals NHS
Foundation Trust

**Myopia Progression in Children with Stickler Syndrome: a
Longitudinal Cohort Study**

Introduction:

As the range of interventions to tackle myopia progression widens, there is increasing appreciation of the heterogeneity of clinical course of early-onset myopia dependent on aetiology. The Stickler syndromes are connective tissue disorders associated with congenital syndromic myopia, and represent the most common cause of rhegmatogenous retinal detachment in children. In this longitudinal study, we aimed to evaluate the progression of myopia in children with genetically-confirmed Stickler syndrome.

Methods:

Inclusion criteria were all patients under 18 years of age with genetic diagnosis of Stickler syndrome and available refractive data, presenting to the NHS England Stickler Highly Specialised Service in Cambridge. Change in spherical equivalent refraction from initial to most recent clinical visit was compared using a paired t-test.

Results:

40 children with Type 1 Stickler syndrome (COL2A1 variant) and 5 patients with Type 2 Stickler syndrome (COL11A1 variant) were included in the study (mean age at presentation 4.71 ± 2.2 years). Mean length of follow-up was 60.2 months. The mean rate of myopia progression was -0.004 ± 1.36 dioptres per year amongst those with Type 1 Stickler syndrome, and 0.082 ± 0.28 dioptres per year in those with Type 2 Stickler syndrome. There was no statistically significant difference between initial and most recent refraction in either group ($p = 0.20$ for each group, paired t-test).

Discussion:

This longitudinal study, representing the largest cohort study of myopia progression in children with a genetically confirmed diagnosis of Stickler syndrome, indicates that there is minimal progression in congenital myopia associated with Stickler syndrome.

**INHERITED
RETINAL
DISEASE**

Zack Soh

Co-Authors:

Mel Maranian.

Vitreoretinal

Research Group

Other*:

Thomas Nixon

Allan Richards.

Howard Martin.

Arabella

Poulson.

Philip Alexander.

Martin Snead.

*NHS England

Highly

Specialised

Stickler

Syndrome

Diagnostic

Service

**Functional analysis of variants of unknown clinical significance in
Stickler syndrome**

Introduction:

Stickler syndrome is an inherited connective tissue disease associated with high-degree myopia and significant risk of retinal detachment. The diagnosis of Stickler syndrome is usually confirmed through a combination of clinical phenotyping allied with molecular genetic analysis. Under the current ACGS variant classification criteria, intronic variants and synonymous substitutions within exons are usually classified as variants of unknown significance when insufficient evidence exists to classify the variant as consistent with a genetic diagnosis of Stickler syndrome. In such instances, functional evidence of a causal association between variant and disease can enable re-classification of such variants.

Methods:

91 patients were identified from the Stickler syndrome clinic at Addenbrooke's hospital, who have a clinical diagnosis of Stickler syndrome but in whom no definitive pathogenic variant was identified according to current best practice guidelines. Variant-containing minigenes from patients were ligated into expression vectors and transfected into MIO-M1 cells. RNA was later extracted to undergo reverse transcription-polymerase chain reaction.

Results:

The minigene splicing assays showed that 47 variants cause damaging effects on the gene product through missplicing leading to exon skipping or intron segment retention. This includes 10 out of 40 variants previously classified as variants of unknown significance, 21 out of 31 novel variants, and 16 out of 20 previously reported variants.

Discussion:

The utility of functional analysis such as minigene splicing assays is not limited to Stickler syndrome, and can provide strong evidence for re-classifying variants of unknown significance as pathogenic.

**LIDS,
LACRIMAL &
ORBIT**

Felicity Allen

Co-Authors:
Robert Brady.
Addenbrooke's
Hospital

Dacryocystorhinostomy Surgery In Patients With Granulomatosis With Polyangiitis

Purpose:

Granulomatosis with polyangiitis (GPA) is a rare systemic vasculitis which commonly effects the upper respiratory tract. This can cause obliteration of the nasal space and resultant nasolacrimal duct obstruction. The resulting symptoms require surgical management with dacryocystorhinostomy surgery. We present the outcomes of dacryocystorhinostomy surgery in GPA patients at Addenbrooke's hospital.

Methods:

In this retrospective study, patients who underwent dacryocystorhinostomy with GPA were identified from the hospital's electronic database. Duration of vasculitis diagnosis prior to surgery, symptoms prior to surgery, immunosuppression at time of surgery, perioperative medical management, complications, resolution of symptoms at follow up and need for further surgical intervention were recorded.

Results:

Nine patients were identified over the study period (2012-2020). Three underwent bilateral surgery; therefore, twelve dacryocystorhinostomy surgeries were performed on GPA patients. 67% of patients had a documented mucocele prior to surgery. 89% were on systemic immunosuppression at the time of surgery. 11/12 of the surgeries were completed with intraoperative intravenous steroid cover. All patients had a postoperative course of oral prednisolone. Mean duration of follow up was 30 months (range 13-54 months). 92% (11/12) of dacryocystorhinostomy surgeries were functioning at follow up. 8% (1/12) had functional failure on follow up; however, anatomical success was noted on nasal endoscopy. Further surgery was not performed due to ongoing poorly controlled vasculitis. One patient had recurrent nasal collapse post operatively requiring surgical correction.

Discussion:

Dacryocystorhinostomy surgery can be successfully performed in GPA patients under additional steroid cover. These patients should be counselled regarding a risk of nasal collapse.

**PAEDIATRIC,
STRABISMUS**

Louise Allen

Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

**The DivO study: is infrared digital imaging more accurate than
ophthalmoscopy for detecting congenital cataract.**

Congenital cataract is the most common cause of avoidable child blindness worldwide. Early detection and management within the first 3 months of life to prevent permanent visual deprivation amblyopia. Although high income countries have well established neonatal screening programmes to evaluate the red-reflex, there is evidence that a third of congenital cataracts are missed and that 90% of specialist referrals are false positives.

Infrared-reflex digital imaging offers potential advantages: lack of pupillary constriction, improved contrast, uniform findings regardless of eye pigmentation and the potential for machine learning and telemedicine.

This presentation will cover the theory and practice behind this new imaging technique, the development of a novel protocol for a paperless study, the use of data linkage for clinical studies and first year results from the national study currently underway.

**PAEDIATRIC,
STRABISMUS**

Louise Allen

Department of
Ophthalmology,
Cambridge
University
Hospitals NHS
Foundation
Trust.

Innovating in Ophthalmology

In our role as clinicians we constantly come across aspects of care and patient administration which could be done better and more efficiently. We are vital in driving and evaluating innovation within the NHS to improve care for our patients, and digital innovation is an integral part of the NHS Long Term Plan

There are many hurdles and barriers to innovating as a clinician and 95% of innovations are never adopted even after significant time and financial investment.

This presentation will describe the pathway between ideation and adoption of innovation using several different ophthalmic digital innovations as examples. It will cover funding streams to support prototype development, proof-of-concept studies and implementation studies; intellectual property; regulatory requirements and routes to adoption.

Innovation is difficult but necessary, it is essential to understand the pitfalls and how to navigate them to ensure patients benefit.

**PAEDIATRIC,
STRABISMUS**

Raisa Ahmed

Co-Authors:

Louise Allen

Department of
Ophthalmology,

Cambridge

University

Hospitals NHS

Foundation

Trust.

Video-consulting with DigiVis testing: a real-world evaluation

Introduction:

DigiVis is a validated CE marked web-app enabling self-testing of distance visual acuity (VA).

Aims:

To describe the implementation of the DigiVis test in remote consultation in the Orthoptic service.

Methods:

Families of children due a follow-up Orthoptic appointment were invited to have a video consultation with synchronous DigiVis VA testing. Inclusion criteria included an age of 4 years or older, a requirement primarily for VA assessment and parental agreement to participate.

Results:

71 families agreed to undertake a remote consultation with DigiVis. The median age was 6 years (range 4-10). 53 (74.6%) children were having amblyopia therapy, the remainder were under observation for refractive error or intermittent tropias. 63 (88.7%) were able to complete the test over Attend Anywhere. Compared to the VA assessment at the subsequent face-to-face consultation the mean bias was 0.01 logMAR with upper and lower Limits of Agreement of +0.12logMAR and -0.10logMAR respectively. DigiVis had 100% sensitivity and specificity in identifying an intra-ocular VA difference (IOD) of 0.05logMAR or more. 47 out of 52 (90.4%) families asked said they could and would like to do asynchronous DigiVis testing in the future.

Conclusion:

Synchronous DigiVis testing during video-consultation can support remote consultation in selected orthoptic patients and is well accepted by most parents. It is accurate at detecting IOD and comparable to standard testing in clinic. Remote consultation with DigiVis testing may reduce time off work and school for families, reducing carbon emissions and releasing clinic space.

**NEURO-
OPHTHALMOLOGY**

Patrick Yu Wai Man

Department of
Ophthalmology, CUH-
NHS Foundation Trust

Gene Therapy for Inherited Optic Neuropathies - Opportunities and Challenges

Inherited optic neuropathies are genetically heterogeneous. The two main groups are Leber hereditary optic neuropathy (LHON) caused by primary mitochondrial DNA (mtDNA) point mutations and autosomal dominant optic atrophy (DOA) caused by mutations in the nuclear-encoded OPA1 gene. Gene therapy is an obvious therapeutic approach aimed at correcting the underlying genetic defect to prevent the ongoing loss of retinal ganglion cells and stabilise or improve vision. Although promising results have been obtained from phase III clinical trials for LHON based on allotopic expression of the MT-ND4 gene for the common m.11778G>A mtDNA mutation, several unexpected issues have emerged calling into question the optimal gene delivery system, the ideal therapeutic window for intervention, and whether interocular transfer of the gene therapy vector can occur. Resolving these controversies will be crucial given the fact that other gene therapy trials are in the pipeline for LHON and OPA1 DOA.

PAEDIATRIC

Thomas Nixon

Co-Authors:

Tasneem Khatib,

CUH

Antoin Safi, CUH

Stylianou

Georgoulas,

CUH

Giovanni

Montesano,

Moorfields Eye

Hospital

Howard Martin,

University of

Cambridge

Allan Richards,

University of

Cambridge

Annie McNinch,

CUH

Arabella

Poulson, CUH

Philip Alexander,

CUH

Martin Snead,

CUH [Lead PI]

Peripapillary Hyper-Reflective Ovoid Mass-like Structures in Stickler syndrome.

Introduction:

Anomalous optic discs are observed in some patients with Stickler syndrome, some of which match the description of peripapillary hyper reflective ovoid mass-like structures' (PHOMS) - an OCT finding in various optic nerve abnormalities.

Methods:

Patients at the Stickler Syndrome highly specialised service with optic disc abnormalities were examined with enhanced depth imaging optical coherence tomography and autofluorescence. The presence of PHOMS was assessed and graded by two independent assessors according to the recommendation of The Optic Disc Drusen Studies Consortium. A third assessor was used in cases of disagreement. The presence of optic disc drusen was also assessed.

Results :

Twenty-two eyes with optic disc abnormalities from eleven patients (eight female, three male; mean age 31 years (range 13-58)) were assessed. PHOMS were present in 91% (n=20 eyes) of imaged eyes. 70% (n=14 eyes) had type 1 Stickler Syndrome and 30% (n=6 eyes) had type 2 Stickler Syndrome. No co-existing optic disc drusen were identified and raised intracranial pressure was excluded after neurological investigation. PHOMS was not specific to particular pathogenic variants, and the presence of PHOMS with a specific pathogenic variant was not predictive of PHOMS in another patient with the same variant. PHOMS was not predictive of the presence or absence of retinal detachment, hearing loss, craniofacial anomalies or arthropathy.

Conclusion:

This is a novel finding of the presence of PHOMS in Stickler syndrome, which should be considered when an anomalous optic nerve is identified, and may suggest a role for collagenopathy in optic nerve disease.

NEURO- OPHTHALMOLOGY

Benson Chen

Co-Authors:

Riddhima Gautam.
Cambridge Clinical
Vision Laboratory,
NIHR Cambridge BRC
Nicholas Cunniffe.
Department of
Neurology, CUH-NHS
Foundation Trust.
Dimitrios
Apostolopoulos.
Department of
Neurology, CUH-NHS
Foundation Trust
Patrick Yu-Wai-Man.
Department of
Ophthalmology, CUH-
NHS Foundation Trust

Seeing Beyond the Eye: Neuro-ophthalmic Endpoints in Clinical Studies of Neurological Disease

Vision is a complex and integrated function that engages a significant proportion of the brain's neural circuitry. As the eye is an extension of the central nervous system, reviewing changes in the structure and function of the eye could lead to the development of non-invasive tests for diagnosing and monitoring neurological diseases, and assessing the impact of treatments as part of routine clinical care or in clinical trials. In Cambridge, neuro-ophthalmic study endpoints are being incorporated in clinical studies of neurological disease, alongside traditional endpoints that emphasise neurological signs and symptoms. Diseases that invariably affect vision or the visual pathways benefit from the inclusion of neuro-ophthalmic study endpoints. Clinical trials of remyelination in patients with multiple sclerosis combine structural measures of the eye obtained from OCT, with functional measures of vision and the visual pathways including psychophysical tests of visual function (low contrast visual acuity, colour vision, and contrast sensitivity function), eye movement recordings, and visual evoked potentials. Clinical studies of patients with Huntington's disease also incorporate structural and functional neuro-ophthalmic endpoints. Preliminary studies have found that impairments in the stability of eye fixation differentiates early and late pre-manifest carriers of the gene for Huntington's disease. Further confirmation of these results may aid in the development of a clinical tool to predict risk of conversion from pre-manifest to manifest disease. Incorporating neuro-ophthalmic study endpoints in clinical studies of neurological diseases offers a promising avenue for advancing our understanding and management of these conditions.

SURGICAL RETINA

Mel Maranian

Co-Authors*:

Thomas Nixon,
Howard Martin,
Martin Snead.

University of

*Cambridge,

John van Geest

Centre for Brain
Repair

Transcriptional changes in physiological and pathological posterior vitreous detachment

Introduction:

The anatomical definition and pathogenesis of posterior vitreous detachment (PVD) remains controversial. Recent research challenges historical concepts that PVD is simply an inevitable consequence of age-related structural changes of the vitreous. Whilst usually uncomplicated, PVD can be a precursor to sight threatening conditions, including retinal detachment (RD), cellophane maculopathy (CM) and macular hole (MH). The factors differentiating physiological (benign) PVD from pathological PVD are poorly understood. A novel cell population (laminocytes) in the posterior hyaloid membrane (PHM), are observed at low density in physiological PVD, and at increased density in patients with pathological PVD. We investigate if differential gene expression (DGE) relates to variations in PVD pathogenesis and its potential association with laminocyte proliferation.

Methods:

Bulk-RNA Next Generation Sequencing (NGS) libraries from >130 vitrectomy samples of patients with physiological or pathological PVD were sequenced and DGE analysis performed. Additionally, spatial transcriptomic analysis was performed on formalin fixed paraffin embedded (FFPE) samples from patients with retinal detachment and cellophane maculopathy.

Results:

Analysis revealed >8000 differentially expressed genes (DEGs) in pathological PVD vs physiological PVD. Over 60% of all DEGs are upregulated in each of the pathological groups. Comprehensive analysis is underway, examining common and unique elements within each dataset. Provisional analysis includes cell adhesion and extracellular matrix organisation pathways related to CM and MH and strong evidence for immune response-regulating signalling pathways involving the genes unique only to physiological PVD.

Discussion:

This research provides a comprehensive representation of the cellular and molecular changes that influence the progression and pathogenesis of PVD.

SURGICAL RETINA

Thomas Nixon

Co-Authors*:

Mel Maranian.

Anton Enright.

Allan Richards.

Howard Martin.

*All University of
Cambridge

RNA-seq suggests integrins as a potential therapeutic target in epiretinal membrane pathogenesis

Introduction:

In idiopathic epiretinal membrane (ERM), fibrocellular tissue contracts and distorts the retinal surface, causing distorted or reduced vision. To investigate the pathogenesis of ERM, RNA-seq was used to analyse the transcriptome in human surgical samples, comparing to control vitrectomy for idiopathic physiological, uncomplicated PVD (uPVD).

Methods:

Membranes peeled from 14 patients with ERM and vitrectomy samples from 5 patients with uPVD had RNA extracted and converted to cDNA using the SMARTseq v4 Ultra Low Input RNA kit. Following library preparation these were sequenced using an Illumina MiSeq. HISAT2 was used to build an index, HTSeq to produce count tables and DESeq for differential gene expression analysis. Reactome path analysis was used for gene ontology.

Results:

RNA was obtained in 13 ERM samples and 3 uPVD samples. cDNA was obtained in 11 ERM samples and 1 uPVD sample. Significant differential gene expression was observed between ERM and uPVD samples. The top three over-represented pathways were 'extracellular matrix organisation', 'integrin cell surface interactions' and 'assembly of collagen fibrils and other multimeric structures'. Manual inspection of these upregulated pathways in ERM identified integrins $\hat{1}\pm-1$, $\hat{1}\pm-3$, $\hat{1}\pm-11$ and $\hat{1}^2-4$.

Discussion:

The identification of upregulation of integrins in ERM is a new and exciting finding. Integrins have a critical role in linking the cell and extracellular matrix and are involved in cell migration and transition from quiescent to proliferative states. Anti-integrin therapies are being investigated for use in diabetic macular oedema and age-related macular degeneration, and this study suggests ERM as another possible indication.