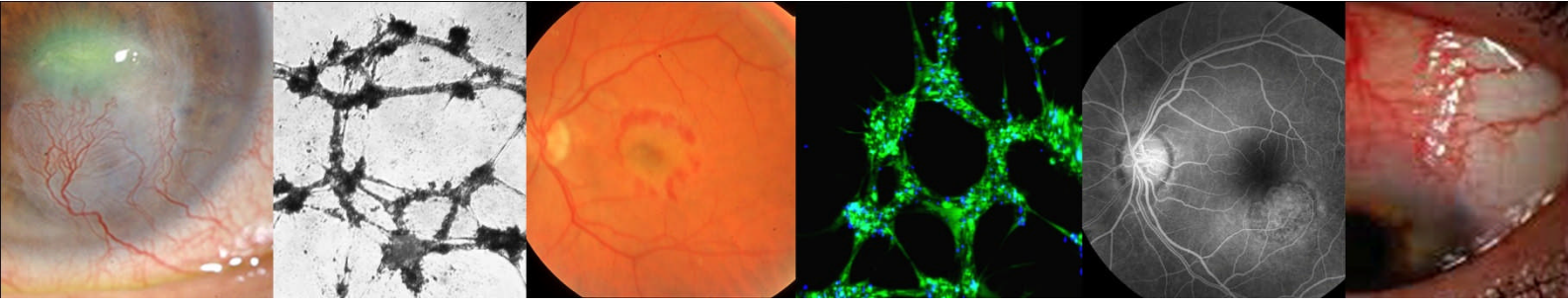

17th Nottingham Eye Symposium and Research Meeting

25th January 2013

Programme and Abstracts

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

NCER Centre for Eye

PROGRAMME CONTENTS

PROGRAMME SUMMARY

8.30am: Registration and Coffee

9.00am: Chairman's Welcome and Opening Remarks

9.10am: Clinical and Translational Research Presentations
Chairs: Mr Winfried Amoaku and Professor Martin Rubinstein

10.30am: Optometry Guest Speaker – Introduction by Professor Martin Rubinstein
Presbyopia: "Are My Eyes Getting Weaker?"
Dr Leon Davies, Aston University

10.55am: Coffee, Trade Stand and Poster Viewing

11.25am: Clinical and Translational Research Presentations continued
Chairs: Dr Andrew Hopkinson and Professor Jean-Jacques Gicquel

12.15pm: In the Pipeline: Sponsor Presentations

12.45pm: Hot Buffet Lunch, Trade Stand and Poster Viewing

1.45pm: 17th Norman Galloway Lecture: New Perspectives in the Management of Ocular Surface Diseases
Professor Jose Gomes, University of São Paulo, Brazil

Symposium on Ocular Neovascularisation
Chairs: Professor Harminder Dua and Mrs Katya Tambe

2.30pm: Corneal Vascularisation: Medical and Surgical Management
Professor Claus Cursiefen, Cologne, Germany

2.55pm: Neovascular Glaucoma: Early Diagnosis and Management
Professor Peter Shah, UCL and Birmingham

3.20pm: Coffee, Trade Stand and Poster Viewing

3.50pm: Retinopathy of Prematurity: What to Look for and How to Treat
Miss Samira Anwar, University Hospitals Leicester

4.15pm: Wet Age Related Macular Degeneration: What's New?
Miss Susan Downes, Oxford University Hospitals

4.40pm: Proliferative Diabetic Retinopathy: Is it History?
Miss Clare Bailey, University of Bristol

5.05pm: Research and Poster Prize Presentations

5.15pm: Chairman's Concluding Remarks and Close of Meeting

5.30pm: CLOSE

See you next year!

9.10AM: CLINICAL AND TRANSLATIONAL RESEARCH PRESENTATIONS, PART 1

Chairs: Mr Winfried Amoaku and Professor Martin Rubinstein

9.10am: Analysis of Visual Fixation Patterns Preceding the Selection of a New Preferred Retinal Locus used in Low Vision Rehabilitation with Microperimetry
Marco Morales, University of Nottingham

9.17am: Corneal Nerves in Eye Bank Preserved Corneas
Virinder Dhillon, University of Nottingham

9.24am: Organization of the Regenerated Nerves in Human Corneal Grafts
Mouhamed Al-Aqaba, University of Nottingham

9.31am: Development of Synthetic Scaffolds for Delivering Limbal Epithelial Cells to the Cornea
Pallavi Deshpande, University of Sheffield

9.38am: Characteristics of Optic Nerve Development using Hand-held Ultra-high Resolution Spectral Domain Optical Coherence Tomography in Premature and Full-term Neonates
Aarti Patel, University of Leicester

9.45am: Characteristics of Infantile Nystagmus using Hand-held Ultra-high Resolution Spectral Domain Optical Coherence Tomography in Infants and Small Children
Helena Lee, University of Leicester

9.52am: Cost Analysis of Goldmann and Tonosafe Disposable Prism Heads
Kirti Jasani, Royal Preston Hospital

9.59am: An Audit of Visual Acuity Measurement and its Consistency within a Large Teaching Hospital
Archana Pradeep, Leicester Royal Infirmary

10.06am: A Bilayered Electrospun Scaffold for Tissue Engineering the Corneal Stroma
Siobhán Dunphy, University of Nottingham

10.13am: Evaluation of Electrospun Gelatin/Polycaprolactone as a Material Suitable for use in Corneal Regeneration
James Rose, University of Nottingham

10.20am: Tight Junction Molecule Expression Permeability and Proliferation in Human Retinal and Choroidal Endothelial Cells in Hyperglycaemia
Saker Saker, University of Nottingham

ABSTRACTS

9.10pm: Analysis of Visual Fixation Patterns Preceding the Selection of a New Preferred Retinal Locus used in Low Vision Rehabilitation with Microperimetry

Marco U Morales, Saker Saker, Rajnikant L Mehta, Martin Rubinstein, Winfried Amoaku

Department of Ophthalmology, Queen's Medical Centre, Nottingham University Hospitals, Nottingham, UK

Background and aims: Patients with pathologies such as age-related macular degeneration (AMD) affecting the central part of the retina may lose their central vision ability altering fixation capabilities.
The rehabilitation of eccentric and unstable vision can be improved by training a new selected retinal locus with better functional characteristics using Microperimetry systems with Biofeedback technology.
The Microperimetry system MAIA (Centervue, Padova Italy), produces estimates of preferred retinal locus (PRL) during the initial 10 seconds of testing (PRL_High), as well as for the entire test time (PRL_Low). The aim of this study was to analyse both fixation loci PRL_H and PRL_L preceding the subjective selection of a new Retinal Locus for eccentric vision training.
Materials and methods: 41 patients, with different diagnosed retinal pathologies, were assessed for fixation characteristics. Each underwent a microperimetry exam with the central 10° and 37 points grid which lasts about 6 minutes. Patients were asked to concentrate their vision on the fixation target (1 degree diameter circle) during the whole exam time. PRL_High (H) is calculated when patients dedicate their highest fixation attention during the first 10 seconds of testing with no interference from microperimetric stimuli projection. The PRL_Low (L) is calculated at the end of the exam from all data available. Automatic estimates of fixation

stability (stable, relatively unstable, unstable) are produced by the instrument based on all available data for the test.
Results: 46 eyes were categorized as stable fixation, 8 as relatively stable and 11 as unstable.
All 11 eyes with unstable fixation and 7 eyes with relatively unstable fixation were found to have their PRL_H and PRL_L in different position with a separation distance from 0.5° to 5° (mean distance = 2.27°, SD = 1.43°). 1 eye with relatively unstable fixation had the PRL_H and PRL_L in the same position, which was the anatomical fovea. 2 eyes with stable fixation had their PRL_H and PRL_L in different position with a separation distance of 0.5° and 1.2°, although in both cases the PRL_L was located inferior from the fovea.
1 eye with unstable fixation had the PRL_H and PRL_L located in the same position 5° superior-nasal from the fovea.
Conclusions: Patients with central and stable fixation have their PRL_H and PRL_L in the same anatomical position which is located over the foveal area showing uniform fixation stability. However, patients, with unstable and relatively unstable fixation may use different retinal zones to fixate during longer task periods. The PRL_H and PRL_L estimates can be used for more precise assessment of fixation stability in two steps during the same fixation attempt. The location of both PRL_H and PRL_L may be considered when selecting a new PRL during the eccentric vision training for better rehabilitation outcomes.

9.17am: Corneal Nerves in Eye Bank Preserved Corneas

VK Dhillon, HS Dua

Department of Ophthalmology, Queen's Medical Centre, Nottingham University Hospitals, Nottingham, UK

Introduction: This is the first and largest study to provide histological evidence that corneal nerves can in fact be preserved in donor corneas when kept in the conventional organ culture storage for several weeks prior to corneal transplant surgery.
Purpose: We aimed to investigate the state of corneal nerves in eye bank preserved corneas using the acetylcholinesterase (AChE) technique.
Methods: 21 eye bank corneas suitable for transplantation were used in this study. Each cornea had been preserved via organ culture storage for 4 weeks at the Manchester Eye Bank. All corneas were stained as whole mounts using the AChE technique; and then scanned enface using the Hamamatsu Nanozoomer digital pathology microscope to view corneal nerves in multiple layers.
Results: A total of 14 of the 21 corneas (66.7%) had AChE positive stromal nerves entering peripherally; of which centrally extending nerves were seen in 8 samples. Many stromal nerves were seen to terminate abruptly. No sub-basal nerves were detected in any of the samples.
Conclusions: Following penetrating keratoplasty, it has been reported that stromal nerves do not contribute to epithelial re-innervation and most sub-basal nerves are seen to regenerate peripherally from the host. Therefore, it has been assumed that the stromal nerves seen in grafts also regenerate from the host. However, since stromal nerves are seen to be present in 66.7% of eye bank corneas prior to transplantation, it is possible that Schwann cell elements from host nerves may guide them to regenerate with donor nerves.

9.24am: Organization of the Regenerated Nerves in Human Corneal Grafts

[1,2] Mouhamed Al-Aqaba, [1] Ahmad Muneer Otri, [1] Usama Fares, [1] Harminder S. Dua.

[1]Division of Ophthalmology and Visual Science, Queens Medical Centre, University of Nottingham, [2]Rotherham Hospital NHS Foundation Trust.

Purpose: To examine by histopathology the degree of nerve regeneration in human corneal grafts and to determine the anatomic organization and morphology of the regenerated nerves.
Methods: Twelve corneal grafts from 12 patients (7 men and 5 women) aged 34-93 (mean, 66.9 years) were included. The most common indication for regrafting was late endothelial failure. The mean duration of graft survival was 6.41 years (range, 1-14 years). The freshly obtained specimens with a narrow rim of host tissue incorporating the graft-host junction were subjected to the acetylcholinesterase method for the demonstration of corneal nerves.
Results: Subbasal nerves were found in 75% and 25% of the grafts at the periphery and center, respectively. They were mostly originated from the host subbasal nerves. Regenerated stromal nerves were detected in

83% of the specimens; half of them showed extension into the center of the graft. A lack of the normal link between the subbasal and stromal nerves was observed and almost all of the regenerated stromal nerves were found to remain within the stroma and did not contribute to the epithelial innervation.
Conclusions: A persistent anatomic disorganization of the corneal nerves in human grafts was found even 14 years after surgery. This could explain the significant reduction of corneal sensation reported in previous studies.

9.31am: Development of Synthetic Scaffolds for Delivering Limbal Epithelial Cells to the Cornea

P Deshpande[1], C Ramachandran[2], F Sefat[1], C Johnson[1], I Mariappan[2], D Balasubramanian[2], AJ Ryan[3], G Vemuganti[4], VS Sangwan[2], S MacNeil[1]

[1]Department of Material Sciences & Engineering, Kroto Research Institute, University of Sheffield, Sheffield, United Kingdom, [2]Sudhakar and Sreekant Ravi Stem Cell Lab, L V Prasad Eye Institute, Kallam Anji Reddy Campus, L V Prasad Marg, Hyderabad, India, [3]Department of Chemistry, University of Sheffield, Sheffield, United Kingdom, [4] School of Medical Sciences, University of Hyderabad, Hyderabad, India

Introduction: One of the many causes of loss of corneal transparency is limbal stem cell deficiency. Several procedures have been developed to prevent blindness by transfer of cultured limbal cells often on an amniotic membrane. The results can be good but the transparency of the cornea is not completely regained and there is a small disease transmission risk in using human donor amniotic membrane. The aim of this project was to develop a synthetic alternative to the amniotic membrane for transferring limbal epithelial cells, both laboratory expanded and from limbal explants for treatment of limbal stem cell deficiency.
Methods: Poly (lactide-co-glycolide) 3D scaffolds were electrospun to produce scaffolds of about 3-5µm diameter fibres and 50-100µm thickness. Human and rabbit limbal epithelial cells were cultured on the scaffolds for one week and explants placed on the scaffolds after which they were placed either cell/explant side down or up on a cornea organ culture and either at an air-liquid interface or submerged for 4 weeks.
Results: Cells transferred from the scaffolds to a rabbit cornea ex vivo model formed a layer 2-3 cells thick after 4 weeks culture. Scaffolds completely degraded within 6 weeks- and degraded faster in the presence of cells.
Conclusion: We suggest that this carrier may be used as an alternative to the amniotic membrane in the treatment of limbal stem cell deficiency reducing the risk of disease transmission to the patient and providing a more reproducible and an off-the-shelf alternative to the amniotic membrane.

9.38am: Characteristics of Optic Nerve Development Using Hand-Held Ultra-High Resolution Spectral Domain Optical Coherence Tomography in Premature and Full-term Neonates

Aarti Patel[1], Helena Lee[1], Viral Sheth[1], Gail Maconachie[1], Frank Proudlock[1], Rebecca McLean[1], Samira Anwar[2], Joe Fawke[3] and Irene Gottlob[1]

[1]Ophthalmology Group, University of Leicester, Robert Kilpatrick Clinical Sciences Building, PO Box 65, Leicester Royal Infirmary, Leicester, LE2 7LX; [2] Department of Ophthalmology, University Hospitals of Leicester, Leicester Royal Infirmary, Infirmary Square, Leicester, LE2 7LX; [3] Department of Neonatology, University Hospitals of Leicester, Leicester Royal Infirmary, Infirmary Square, Leicester, LE2 7LX

Purpose: Development of the optic nerve in the neonatal period is unclear. Previous studies suggest that prematurity is associated with optic nerve hypoplasia. This is the first study to describe the development of the optic nerve in infants born prematurely in comparison to full-term infants using ultra-high resolution spectral domain hand-held OCT (HH-OCT).
Methods: A mixed cross-sectional and longitudinal study design was adopted. 34 infants were recruited to the study: 23 premature infants born at 24-30 weeks gestation and 11 full-term infants born at 37-42 weeks. Each patient underwent an ophthalmological examination and a HH-OCT scan (Bioptigen, 2.6µm axial resolution) without sedation. The premature infants underwent longitudinal follow up scans on an average of 2 occasions up to 46 weeks gestational age. The full-term infants were examined once within the first week. The optic nerve was analysed using ImageJ Software and linear mixed model analysis with SPSS v20 Software.

Results: The optic cup/disc ratio demonstrated a reduction with age of examination in premature infants ($p<0.001$) on both cross-sectional and longitudinal imaging due to decreasing cup width ($p<0.05$) and increasing disc width ($p<0.05$). The optic disc rim also showed increasing width with age of examination ($p<0.001$). Increasing gestational age at birth was associated with deepening of the optic cup in both premature and full-term infants.
Conclusions: This is the first study to analyse early optic nerve development in premature and full-term infants using HH-OCT. Our results suggest prematurity is associated with significant differences in optic nerve morphology in premature infants as compared to full-term infants.

9.45am: Characteristics of Infantile Nystagmus using Hand-Held Ultra-High Resolution Spectral Domain Optical Coherence Tomography in Infants and Small Children

Helena Lee[1], Viral Sheth[1], Mashal Bibi[1], Gail Maconachie[1,] Aarti Patel[1,] Frank Proudlock[1], Christopher Degg[2], Rebecca McLean[1], Jonathan Aboshiha[3,4], Venki Sundaram[3,4], Anthony Moore[3,4], Michel Michaelides[3,4], Mervyn Thomas[1], Samira Anwar[5], Nagini Sarvananthan[5] and Irene Gottlob[1]

[1]Ophthalmology Group, University of Leicester; [2]Department of Medical Physics, University Hospitals of Leicester, [3]UCL Institute of Ophthalmology, University College London, [4]Moorfields Eye Hospital, [5]Department of Ophthalmology, University Hospitals of Leicester, Leicester Royal Infirmary, Infirmary Square, Leicester, LE2 7LX

Purpose: To investigate the feasibility and clinical use of ultra-high resolution spectral domain hand-held OCT (HH-OCT) in a systematic study of pathological foveal development in a cohort of infants and young children with nystagmus.
Methods: 50 patients were recruited and compared to 50 age matched controls. The mean age was 3.2 ± 2.0 years (range 0-8). Each patient had a full orthoptic and ophthalmological examination, and a HH-OCT scan. Each scan was screened for the presence of foveal hypoplasia and other abnormalities of macular morphology. A differential diagnosis was made on the basis of OCT findings and correlated with clinical, genetic and electrophysiological findings.
Results: Scans were obtained in 94% of cases at the first examination and 100% at the second examination. Twenty-three patients had typical foveal hypoplasia. Of these, 21 had albinism and 2 had PAX6 mutations. Five patients had atypical foveal hypoplasia and were diagnosed with achromatopsia. Six cases with retinal dystrophy had other abnormal macular morphology. The remaining 16 patients had normal scans. Of these, 12 had idiopathic nystagmus and 4 had latent nystagmus.
Conclusion: Excellent feasibility of the HH-OCT in this challenging cohort has been demonstrated. Examining OCT scans for the presence of typical or atypical foveal hypoplasia and other abnormal macular morphology, is helpful in the differential diagnosis of infantile nystagmus. This may facilitate more focused investigations and earlier diagnosis, which is important in an era where potentially time sensitive interventions such as gene therapy are being undertaken.

9.52am: Cost Analysis of Goldmann and Tonosafe Disposable Prism Heads

Jasani KM, Morarji J, Sattar N, Putri C, Pearl A, Mercieca K, Bhargava A.

Royal Preston Hospital, Sharoe Green Lane, Fulwood, Preston, PR2 9HT.

Introduction: A recent USA based study showed almost equivalence of cost between the use of disposable Tonosafe heads and Goldmann prism heads. The authors feel that this analysis is flawed due to assumptions including that departments replace their Goldmann tonometer heads after 100 uses and have recalculated the findings based on a survey of UK practice.
Methods: A telephone survey of current UK practice with regards to use of disposable/non disposable heads was undertaken. Based on the findings a cost analysis was undertaken to compare the most cost-effective alternative.
Results: Initial findings show that the predominant UK practice is replacement of Goldmann prisms on damage or loss rather than after 100 uses. We also found a mean rate of replacement of prism heads of 23.6% per department per year (range 0% to 50%). Based on this the 5-year cost of using Goldmann prisms was £18,125 compared with £2,313 for Tonosafe.

Discussion: The authors feel this is a more realistic cost analysis of use based on current UK practice. The relative cost benefits may still be outweighed however by litigation over injury or infection sustained with use of non-disposable prism heads.

9.59am: An Audit of Visual Acuity Measurement and its Consistency within a Large Teaching Hospital

A.Pradeep (MBBS,MD), A.Morawski(Msc),H.Chauhan(Msc,orthoptics) J.Burns,Frcophth.

Leicester Royal Infirmary

Introduction: Is visual acuity being measured consistently by all members of staff, and is accuracy affected by where the test is performed? Inaccurate testing of this fundamental part of the ophthalmic examination could result in treatment or services being denied to eligible patients.
Purpose: To assess visual acuity recording practices and identify any measurement discrepancies and/or patterns; to ascertain if such discrepancies are attributable to technique, equipment, or both.
Methods: Prospective data collection, using 4 different methods: inventory of equipment, direct observation, staff questionnaires and volunteer testing. Sample size of 39 charts and 29 staff who regularly perform visual acuity testing on adult patients.
Results: Patient-to-chart distance varied from 3.4m to 8.7m, with 12 of which showing deviation of <10cm from 6m, whilst 20 showed < 30cm deviation. Occlusion methods and the level of encouragement varied between different staff groups. When a patient was unable to read 6/60 only 18% of staff were observed attempting testing at a shorter distance, opting instead to test for c/f vision; this in spite of the responses in the questionnaire, where 93% stated they would test at the shorter distance. Volunteer testing showed differences of around 2 lines between charts, and trends showed clearly the same charts consistently giving worse or improved acuity.
Conclusions: Results primarily from inventory and volunteer testing demonstrate problems caused by positioning and illumination of charts, resulting in inaccurate and inconsistent readings. Staff technique varies dependent upon training, staff group, and is strongly influenced by time pressures and constraints. Both issues are of great significance, considering the visual acuity is an assessment criterion for treatment of cases such as ARMD and cataracts.

10.06am: A Bilayered Electrospun Scaffold for Tissue Engineering the Corneal Stroma

S Dunphy[1], H Dua[2], A El Haj[3], A Hopkinson[2], F Rose[4]

[1]EPSRC DTC for Regenerative Medicine, School of Pharmacy, University of Nottingham, UK. [2]Division of Ophthalmology and Visual Sciences, University of Nottingham, UK. [3]ISTM, Keele University, UK. [4]Wolfson Centre for Stem Cells, Tissue Engineering and Modelling (STEM), School of Pharmacy, University of Nottingham, UK.

Introduction: Corneal blindness affects millions worldwide. Donor shortages and graft rejection have prompted the search for a tissue-engineered alternative to traditional cadaveric transplants. Electrospun poly (lactide-co-glycolide) (PLGA) was explored as a possible candidate material in the development of a corneal stroma replacement. In vivo, corneal epithelial cells adhere to a basement membrane that presents pores and fibres in the range of 20-400 nm. The nano-scale topography plays a crucial role in directing cellular behaviour. Conversely, corneal stromal cells are interspersed throughout a collagenous ECM. As such, the geometry of PLGA electrospun scaffolds was studied as a means of influencing the behaviour of two distinct corneal cell types.
Results: Electrospun scaffolds were fabricated with average fibre diameters in the micron and sub-micron range, 3 µm and 250 nm, respectively. The biocompatible, biodegradable scaffolds demonstrated appreciable tensile properties capable of withstanding relevant physiological conditions and surgical manipulation. They supported adhesion and proliferation of both primary human corneal stromal mesenchymal stem cells (MSC) and immortalised human corneal epithelial cells (HCEC). The nano-scale fibres provided a surface onto which HCEC could spread across and establish a confluent monolayer while the microfibres facilitated favourable infiltration of MSC.

Conclusion: Data so far suggest a bilayered scaffolding approach may be appropriate for the cornea. A microfibrous scaffold to provide the stromal-type environment into which cells can infiltrate with a nanofibrous layer on top to act as a pseudo basement membrane.

10.13am: Evaluation of Electrospun Gelatin/Polycaprolactone as a Material Suitable for use in Corneal Regeneration

James B Rose, David J Williams, Alicia El Haj, Harminder S Dua, Felicity RAJ Rose, Andrew Hopkinson

University Of Nottingham

Purpose: There is currently a clinical need for synthetic, artificial corneal tissue capable of dampening inflammation, reducing neovascularisation and stabilising the hostile ocular surface environment in patients suffering corneal transplant rejection.
Herein the authors evaluate *in vitro*, the suitability of electrospun gelatin/polycaprolactone sheets seeded with human corneal stromal cells (HCSC) as a potential candidate for preclinical development.
Methods: Scaffolds were electrospun from blends of gelatin and polycaprolcatone at various ratios (100:0, 50:50, 25:75, 0:100 – Gelatin: PCL). Scaffolds were characterised by scanning electron microscopy (SEM), Infra-red spectroscopy, Water contact angle, and histology. Adhesion and Proliferation of HCSCs on selected scaffolds were quantitatively assessed through the AlamarBlue© assay.
Results: The four blends of gelatin: PCL were electrospun with a range of fibre morphologies and in turn significant variation in fibre diameter the mat thickness was relatively well controlled; measuring 60–85µm. HCSCs adhered best to scaffolds made purely of gelatin but proliferated at similar rates on all electrospun scaffolds.
Conclusion: This work demonstrates that gelatin: PCL blends can be electrospun with modest control and that the electrospun sheets possess good cell compatibility. Although far from clinical development, this work represents a good starting point, and a lead into assessing phenotype stability of HCSCs in response to these scaffolds.

10.20am: Tight Junction Molecule Expression, Permeability and Proliferation in Human Retinal and Choroidal Endothelial Cells in Hyperglycaemia

Saker Saker, Elizabeth Stewart, Winfried Amoaku

Division of Ophthalmology and Visual Sciences, University of Nottingham

Purpose: To determine, *in vitro*, the effects of hyperglycaemia on the proliferation and/or alteration in tight junction molecule expression of the human retinal and choroidal micro-vascular endothelial cells as well as compare the permeability of CEC and REC in normo- and hyper-glycaemic conditions.
Methods The expression of the selective tight junction proteins (Occludin, Claudin-5, VE-Cadherin, JAM-A and JAM-C) by CEC and REC under normal and hyperglycaemic conditions was assessed by western blot analysis. Permeability was assessed by the measurement of Evan's blue-labeled albumin transgression across the EC mono-cell layer in trans-wells using a multi-scan plate reader. Proliferation of the EC under the different conditions was determined with a colorimetric assay using WST-1.
Results Although Occludin and JAM-C were expressed in both REC and CEC under normoglycaemia, their expression was significantly different between the 2 cell types with much more expression in REC under normoglycaemia compared to hyperglycaemia. Claudin-5, VE-Cadherin and JAM-A were also expressed in these cells although at a slightly weaker intensity than Occludin. There was a significant difference between the mean permeability rate in hyperglycemia and normoglycaemia with regard to REC. There was a statistically significant reduction in the proliferation of both REC and CEC cultured in hyperglycaemia compared to normoglycaemia.
Conclusions: CEC and REC have different expression profiles of TJ molecules in normoglycaemia. Alteration of TJ molecule expression by hyperglycaemia is different for REC and CEC. Exposure of human RECs to hyperglycaemia for 72 hours or longer results in significant reductions in the expression of selective tight junctions (Occludin, JAM-C) as opposed to the slight alterations observed in choroidal cells. Reduced proliferation of REC and CEC in hyperglycaemia is likely to play an important role in diabetic eye disease. Retinal and choroidal vascular occlusions in diabetic eye disease are due to reduced EC proliferation. The

relative rarity of choroidal neovascularisation in advanced diabetes is explained. The paradoxical retinal angiogenesis in advanced diabetic retinopathy is most likely due to secondary changes occurring in diabetic retinopathy.

10.30AM: OPTOMETRY GUEST SPEAKER:

DR LEON DAVIES, ASTON UNIVERSITY. **PRESBYOPIA: "ARE MY EYES GETTING WEAKER?"**

Leon undertook his optometry degree at Aston University in 1997 and was awarded a First Class Honours. He subsequently attained membership of the College of Optometrists and registered with the General Optical Council. Leon returned to Aston University in 2001 to work on his PhD, and was appointed as lecturer in 2005, and promoted to senior lecturer in 2009. In 2005, Leon was also awarded Fellowship of the American Academy of Optometry. He recently served a term as Clinical Editor for the professional optometry journal *Optometry Today* (OT), and is now a member of OT's Editorial Board. Leon's research interests are centred on ocular accommodation and presbyopia. He was awarded the inaugural College of Optometrists Research Fellowship Award for a study examining *in vivo* 3-D Magnetic Resonance Imaging of crystalline lens morphology in phakic eyes during accommodation, and the Neil Charman Medal for research in optometry, optics and vision science. Leon is also convener of the Ophthalmic Research Group, and is the Ageing Eye Cluster Lead for the Aston Research Centre for Healthy Ageing. More recently in 2012, Leon was awarded Fellowship of the College of Optometrists.

Presbyopia is a ubiquitous condition that manifests during midlife, and is arguably one of the best chronological indicators of ageing. Attempts have been made to restore accommodation to the ageing eye, but with limited success. Current surgical techniques rely on the persistence of the accommodative mechanism throughout life; however, the exact aetiology of presbyopia remains elusive. This presentation will, therefore, describe the age-related physiological changes to the accommodation system observed before, during and after the onset of presbyopia.

11.25AM: CLINICAL AND TRANSLATIONAL RESEARCH PRESENTATIONS, PART 2

Chairs: Dr Andrew Hopkinson and Professor Jean-Jacques Gicquel

11.25am: ***Keynote Research Presentation:***
Hartmann-Schack Aberrometry and OQAS, the quest for the New Frontier in Vision Quality
Professor Jean-Jacques Gicquel, Poitiers, France

11.40am: Development of Tissue Engineered Microenvironments for Corneal Repair
Ílida Ortega, University of Sheffield

11.47am: Peptide Amphiphiles as Versatile Substrates for Oriented Cell Adhesion and Proliferation of Human Cornea Stromal Keratocytes
Ricardo M. Gouveia, University of Reading

11.54am: Localiastion of Yap/Taz in Corneal Epithelia: A Marker of Mechano-Sensitivity and Role in Epithelial Homeostasis
Che Connon, University of Reading

12.01am: The Effects of Gravitational Force on Limbal Stem Cell Transplants
Ammar Miri, Nottingham University Hospitals

12.08am: Characterisation of Cultured Stromal Cells: *In vitro* Restoration of the Keratocyte Phenotype using Co-culture Approaches
Samantha Wilson, Keele University

11.25am: Keynote Research Presentation:
Hartmann-Schack Aberrometry and OQAS, the Quest for the New Frontier in Vision Quality
Professor Jean-Jacques Gicquel, Poitiers, France

Professor Jean-Jacques GICQUEL, MD, PhD, FEBO
Is the Department Head of ophthalmology of the Saintes and Saint Jean d'Angely Hospitals, Professor of Ophthalmology, Poitiers School of Medicine, France. He was a Cornea Fellow and House Surgeon in Professor Paul Dighiero's ophthalmology department, Poitiers, France. He was invited to chair the department of ophthalmology of the Saintes and Saint Jean d'Angely Hospitals in 2003 and taking part in the building of a large ophthalmology federation for the south-west region of France. His clinical subspecialty interest is in Cornea and Ocular Surface and his research interests are in Ocular Immunology, Corneal Wound Healing and the study of the Quality of Vision. He was a full time researcher in Professor's Dua's "Ocular surface tissue laboratory" at the Queens Medical Centre, Nottingham, United Kingdom from 2006 to 2007. In charge of the stem cell therapy projects in ophthalmology in Jean Bernard University Hospital, Poitiers, France, he has been developing several novel surgical procedures and management protocols in, amongst others, corneal epithelial stem cell grafting and amniotic membrane. He has developed new ways to study dynamically the quality of vision and in 3D. He is the author of more than a hundred and fifty research presentations, publications, and book chapters in international congresses and journals. He is also a section editor of the British Journal of Ophthalmology and a member of the board of Acta Ophthalmologica.

The talk will start by defining the concept of quality of vision (a new frontier that goes beyond visual acuity). Then I will show how techniques, first developed for *ASTRONOMICAL* applications and defense, give the ophthalmologist new tools, to measure the quality of vision, in healthy subjects and patients. I will go thru the pros and cons of each of the devices, developed for this very purpose and show their current applications. I will finally present new techniques, studying the quality of vision dynamically, in 3D and giving the patient a "preview" of a potential surgical procedure on his quality of vision.

11.40am: Development of Tissue Engineered Microenvironments for Corneal Repair

Ílida Ortega[1], Anthony J. Ryan[2], Pallavi Deshpande[1], Sheila MacNeil[1] and Frederik Claeyssens[1]

[1] Biomaterials and Tissue Engineering Group, Department of Materials Science and Engineering, Kroto Research Institute, University of Sheffield, Sheffield, United Kingdom [2] Department of Chemistry, University of Sheffield, Sheffield, United Kingdom

Purpose: Corneal blindness occurs as a result of limbal epithelial cell (LEC) deficiency due to causes such as chemical burns, Aniridia, radiation or multiple surgeries. LECs are located in the limbus at the Palisades of Vogt in specific microenvironments or stem cell niches.
Our aim is to develop experimental models of the limbus in which to study LEC activity. Specifically, we have designed two types of microfabricated corneal outer rings (one biodegradable and other non-biodegradable) containing micropockets to simulate LEC microenvironments.
Methods: The non-biodegradable rings were made of polyethylene glycol diacrylate (PEGDA) using photopolymerisation microstereolithography. The biodegradable rings were made of poly (lactic-co-glycolic acid) 50:50 using a novel technique combination of microstereolithography and electrospinning. Both models presented microfeatures of sizes around 300 μm.
Preliminary work on the evaluation of the constructs was performed using both limbal tissue explants and rabbit limbal epithelial and stromal cells. The potential use of the rings as cell delivery devices was evaluated using a 3D rabbit cornea model. Moreover, cells were characterized in both types of constructs using CK3 (differentiation marker) and P63 (stem cell marker).
Results: In both cases we demonstrated that cells attach and proliferate on the constructs; we specifically located cells in the artificial micropockets and for both approaches we obtained promising results regarding epithelial cell transfer and re-epithalisation of damaged corneas using a 3D rabbit model.

Conclusion: This work provides a technique for producing artificial niches for studying LEC behaviour *using* in *vitro* and *ex vivo* models. Both biodegradable and non-biodegradable rings could be potentially used as stem cell carriers for the treatment of corneal disease.

11.47pm: Peptide Amphiphiles as Versatile Substrates for Oriented Cell Adhesion and Proliferation of Human Cornea Stromal Keratocytes

Ricardo M. Gouveia; Valeria Castelletto; Ian Hamley; Che J. Connon

School of Chemistry, Food and Pharmacy, University of Reading, United Kingdom

Purpose: To develop novel bioactive surfaces able to support adhesion and proliferation of human corneal stroma keratocytes (HCSK) in vitro whilst emulating the cell's in vivo phenotype. This includes maintaining proper cell morphology, the expression of specific HCSK markers, and the aligned deposition of collagen type-I. To this purpose, we developed peptide amphiphile (PA) molecules composed by a hexadecyl lipid chain attached to a peptide headgroup comprising the integrin-binding motifs RGD or RGDS, or the negatively charged ETTES sequence.
Methods: PAs were studied by transmission electron microscopy, small-angle X-ray scattering, and X-ray diffraction. In addition, fluorescence spectroscopy was used to determine the critical concentration for PA self-assembly (c.a.c.) in water. PA solutions at 1×10^{-2}-10^{-4} M and at various RGD(S):ETTES molar ratios were dried and used as coatings to enhance HCSK adhesion, viability, and proliferation. Furthermore, the effect of these PA substrates on the expression of HCSK markers was evaluated by QPCR.
Results: Above their c.a.c. (>0.01 wt%), PAs formed well-defined, stable nanotapes, with bilayer structures and β-sheet features. When used as coating substrates, PAs containing the RGD(S) motifs were bioactive, specifically promoting integrin-dependent adhesion and proliferation of HCSKs without significantly altering the expression patterns of analysed keratocyte markers. However, no adhesion was observed with ETTES coating alone. Optimal adhesion and maximal cell proliferation was achieved with 1.25×10^{-3} M RGDS:ETTES at 13:87 (mol/mol) ratio. This binary system enhanced adhesion 1.4-fold relatively to substrates composed of only the RGD or RGDS molecules, suggesting that spacing between RGD(S) motifs promotes cell adhesion, whilst epitope crowding impairs it.
Conclusions: Self-assembling nanostructures formed by co-assembly of RGD(S)-displaying PAs may constitute a versatile tool for corneal tissue engineering through modulation of HCSK adhesion and proliferation.

11.54am: Localiastion of Yap/Taz in Corneal Epithelia: A Marker of Mechano-Sensitivity and Role in Epithelial Homeostasis.

Che J Connon, Roanne R Jones and James Foster

Stem Cells and Nanomaterials Laboratory, School of Pharmacy, University of Reading

Purpose: To investigate the cellular location of the nuclear transcription factor Yap/Taz (regulator of mechanotransduction) in limbal and central corneal epithelial cells and relate this expression to changes in corneal stiffness centripetally across the ocular surface.
Methods: The localisation of Yap/Taz, CK3, CK14 and ZO-1 across the ocular surface of bovine corneas was examined by immunohistochemistry. Limbal stem cells were isolated form fresh bovine corneas and expanded upon type I collagen gels of differing stiffness for 14 days. The localisation of Yap/Taz, CK3, CK14 and ZO-1 was examined by immunohistochemistry within these corneal constructs. Furthermore, the transcription levels of Yap/Taz, CK3 and ABCG2 were quantified by QPCR
Results: Across the healthy bovine cornea Yap/Taz was predominately expressed cytoplasmically within the limbus, where as in central corneal epithelial cells Yap/Taz was retained within the nucleus. Isolated limbal epithelial cells expanded upon the more compliant collagen gels showed significantly less gene expression of Yap/Taz, which was predominately cytoplasimic at the protein level, whereas more nuclear expression was seen within epithelial cells expanded upon the stiffer collagen gels. This corresponded with more cells expressing cytokeratin 3 and ZO-1 and less cytokeratin 14 and ABCG2 at the gene and protein level.
Conclusions: The nuclear to cytoplasmic expression ratio of Yap/Taz between limbal and central epithelial cells supports our hypothesis of a centripetal stiffness gradient across the corneal surface is likely to underpin new directions in corneal wound healing and our understanding of ocular surface homeostasis.

12.01am: The Effects of Gravitational Force on Limbal Stem Cell Transplant

Miri A, Hashmani K, Al-aqaba M, Faraj LA, Fares U, Otri AM, Said DG, Dua HS.

Nottingham University Hospitals, Nottingham, UK

Aim: To evaluate the effect of gravity on corneal epithelial cell migration *in vitro*.
Methods: Fourteen donor peripheral corneoscleral rims were used. Twenty explants were chosen of which 10 were placed vertically and 10 were placed horizontally during culture. Analyses were performed to investigate the effect of gravity on epithelial growth by measuring the extent of epithelial cell growth above and below the horizontal meridian and counting the total number of cells using a haemocytometer.
Results: There was no statistically significant difference in cell growth between the explants that were placed horizontally and vertically. However, in the vertical explant group the cells grew preferentially towards the 6 o'clock direction, possibly as a result of gravity.
Conclusions: Gravitational forces may influence cell migration *in vitro*. This could be of significance in the planning of limbal transplantation, because a superior graft may be more likely to succeed than a gravitationally challenged inferior graft.

12.08am: Characterisation of Cultured Stromal Cells: *In vitro* Restoration of the Keratocyte Phenotype using Co-culture Approaches

Samantha L Wilson, Ying Yang and Alicia J. El Haj

Institute for Science and Technology in Medicine, School of Medicine, Keele University

Purpose: *In vivo,* epithelial cells are in close contact with keratocytes in the stromal layer; they are connected both anatomically and functionally and it is these interactions that are vital to the maintenance of tissue homeostasis and transparency. Co-culture studies aim to recapture this cellular anatomy and functionality by bringing together two or more cell types within the same culture environment, enabling them to interact and communicate. By more closely mimicking the *in vivo* cellular niche environment we are able to aid our understanding of corneal wound healing mechanisms and the importance of cell mediated interactions; thus enabling us to engineer corneal tissue with stromal cells that are in a healthy, native, uninjured state.
Methods: Three different co-culture methods have been examined; epithelial direct explant; transwell; the use of conditioned media and their effects on stromal cell function were studied. The different co-culture models help us to determine as to whether cell-cell interactions are due to direct cell contact or not, and as to whether the cells themselves have to be present to elicit a response.
Results: We have demonstrated that it is possible to revert cultured corneal stromal cells that are fibroblastic in lineage towards the native uninjured cell type in terms of cell behaviour and biological properties.
Conclusion: This method of activating corneal keratocytes into their fibroblastic lineage and then being able to differentiate them back to the keratocyte lineage is vital to corneal tissue engineering with its benefits being threefold; firstly, it allows for sufficient numbers of corneal stromal cells to be grown up quickly and easily in serum-containing media; secondly the ability to differentiate the expanded activated cells back to a keratocyte linage is important in aiding our understanding of corneal wound healing mechanisms and the importance of the cell interactions during these processes; and finally it allows us to engineer corneal tissues that more closely mimic the native cornea, with cells that are in a healthy uninjured state which may have the potential to act as an important tool in with regards to toxicity testing of drugs and irritants which could in turn improve the development of new and improved ocular drugs to treat corneal disease and/or injury.

12.15PM: IN THE PIPELINE

Updates on the most exciting new products coming to the market from some of our faithful sponsors

12.15pm: **Retina - Catch, Match, Track & Treat,** *Instinctive*

12.20pm: **Yellox™ & New Mimins: Povidone Iodine,** *Bausch & Lomb*

12.25pm: **New Retinal Imaging Modalities for the Heidelberg Spectralis***, Heidelberg Engineering*

12.30pm: **A special update from Moorfields Pharmaceuticals,** *Moorfields Pharmaceuticals*

12.35pm: **Deep Range Imaging… Seeing is Believing,** *Topcon*

1.45PM: THE 17TH NORMAN GALLOWAY LECTURE

PROFESSOR JOSÉ ALVARO PEREIRA GOMES, MD PHD

Professor José Alvaro Pereira Gomes (MD, PhD) completed his medical degree and residency in ophthalmology at Santa Casa Medical School, São Paulo/Sp, Brazil. He then travelled to The Wills Eye Hospital, Philadelphia, USA to undertake a Fellowship in Cornea and External Diseases followed by a Fellowship in Basic Research. After completing an Observer Fellowship in Ocular Immunology at Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, USA he returned to São Paulo to complete his Master and Doctor titles. In 2008 José Gomes became Professor of Ophthalmology in the Department of Ophthalmology, Unifesp/Escola Paulista De Medicina in São Paulo, Brazil. Professor Gomes' is currently an Associated Professor, Professor of the PhD program and Director of the Anterior Segment Area, Advanced Ocular Surface Center and the Cornea and External Diseases Fellowship at the Instituto Suel Abujamra, São Paulo, Brazil.

In his illustrious career Professor Gomes has published over 100 papers in peer-reviewed journals, won 23 awards and honors and presented more than 250 papers and posters at scientific meetings. He is the author of the "Doenças Da Superfície Ocular – Diagnóstico E Tratamento", and has contributed chapters to 58 other ophthalmology books. In addition, he has been on the board of directors of the Cornea Society and is currently the President of the Panamerican Cornea Society and the Brazilian Dry Eye Patients Association (APOS).

The lecture *"New Perspectives for the treatment of Ocular Surface Disease"* aims to present the most recent clinical and surgical therapies for the treatment of challenging conditions that accompany ocular surface diseases. As clinical treatment, new anti-inflammatory medications, antiangiogenic drugs and the use of scleral contact lenses will be reviewed. As more invasive/surgical treatment, the use of biologic adhesives, amniotic membrane transplantation, cell/genetic therapy and new modalities of stem cell transplantation will be discussed.

THE HISTORY

The Norman Galloway Lecture was endowed in 1996, by Mr Nicholas R Galloway, Consultant Ophthalmologist at the University Hospital Queen's Medical Centre Nottingham (retired 2001), in memory of his father. This has since become a key feature of what is now a nationally recognised symposium.

Norman Patrick Galloway was born at Rhynie in Aberdeenshire on 27th March 1895 and died in Rempstone near Loughborough, Leicestershire on 2nd February 1976. He was a graduate of the University of Edinburgh and became a House Physician in the Edinburgh Royal Infirmary. During the First World War he served with the Army in South Africa, afterwards deciding to take up Ophthalmology. He obtained his DOMS in Oxford and during his time in Oxford met his future wife Eileen Thompson, the daughter of a general practitioner in Nottingham.

In 1922 he was appointed Clinical Assistant to the Nottingham and Midland Eye Infirmary and five years later, in 1927, he was elected Honorary Surgeon. He held this appointment through World War II and, in 1948, with the advent of the National Health Service, became Consultant Ophthalmologist. In the 1920's, Norman Galloway was an active member of the British Medical Association and helped to organise the meeting that was held in Nottingham in 1926. At a national level, for many years he supported the Midland Ophthalmological Society, regularly presenting papers, and in 1951 was appointed their President. He was also a member of the Council of the Oxford Ophthalmological Congress. He saw the introduction of antibiotics and steroids and, during the difficult post-war period, helped to steer the Hospital House Committee through the numerous negotiations involved with the formation of the National Health Service. He was also instrumental

in gaining funding for the Eye Hospital extension to the wards and outpatient department. From 1950 to 1951 he was President of the Nottingham Medico-Chirurgical Society.

During his working life, Norman Galloway saw and helped to implement great changes in the practice of Ophthalmology in Nottingham. The old outpatient system where the doctor stood by a desk facing a queue of patients was replaced by consulting rooms and the building of the new extension allowed the introduction of special clinics. Nottingham had an Ophthalmic Nursing School before the war and at an early stage had an Orthoptic Department. Norman Galloway retired from the hospital in March 1959 after 34 years of service. His patients remember him as a kindly man who preferred one-to-one relationships. He tended to avoid public speaking whenever possible.

Nicholas R Galloway

PREVIOUS NORMAN GALLOWAY LECTURES

2012: Professor Irene Gottlob, University of Leicester. *What is moving in Nystagmus?*

2011: Professor F Kruse, Erlangen, Germany. *Descemet Membrane Endothelial Keratoplasty, the Thinner, the Better*

2010: Professor D Wong, University of Liverpool and Hong Kong. *East and West*

2009: Prof IG Rennie, Sheffield. *The Good, the Bad and the Ugly: The Metastatic Potential of Uveal Melanoma*

2008: Professor A Fielder, London. *Paediatric Ophthalmology – Where Next?*

2007: Professor J-J De Laey, Ghent, Belgium. *Paraneoplastic Retinopathies*

2006: Mr JKG Dart, Moorfields Eye Hospital, London. *When Topical Steroids Fail: Managing Severe Anterior Segment Inflammation*

2005: Professor D Azar, Massachusetts Eye Infirmary, Harvard University, Boston, USA. *Wavefront-guided Keratrorefractive Surgery: Advantages and limitations*

2004: Professor R Hitchings, Moorfields Eye Hospital, London. *Normal Tension Glaucoma*

2003: Professor CNJ McGhee, University of Auckland, NZ. *Exploring the Topographic and Inner World of the Cornea to the Horizon of the Iris Plane: Contemporary Imaging of the Anterior Segment of the Eye*

2002: Professor AC Bird, Institute of Ophthalmology, University College London. *Prospects of Treating Inherited Retinal Diseases*

2001: Professor JV Forrester, University of Aberdeen. *Classification and Treatment of Posterior Uveitis*

2000: Professor PR Laibson, Wills Eye Hospital, Philadelphia, USA. *Herpes Simplex Viral Keratitis : What HEDS (Herpetic Eye Disease Studies) has Taught us*

1999: Mr JRO Collin, Moorfields Eye Hospital, London. *Management of Traumatic Ptosis*

1998: Professor LA Donoso, Wills Eye Hospital, Philadelphia, USA. *Stargardt's Macular Degeneration*

1997: Professor DB Archer, Queen's University, Belfast. *Diabetic Retinopathy – a Tolerable Disease*

2.30PM: 17TH NOTTINGHAM EYE SYMPOSIUM 'OCULAR NEOVASCULARISATION'

Chairs: Professor Harminder Dua and Mrs Katya Tambe

This year the symposium has the theme 'Ocular Neovascularisation'. Ocular neovascularisation 'abnormal or excessive formation of blood vessels in the eye' is a topic of wide interest to all Ophthalmologists and Optometrists. Ocular neovascularisation is a major cause of visual loss; with its links to all manner of diseases from age-related to infectious and occurring as a complication of ocular interventions, from contact lens wear to surgery. We have invited speakers from all over the UK and from Germany to give an update on the current understanding and treatment of ocular neovascularisation. The topics that will be covered span a wide range of implications, Professor Claus Cursiefen, Cologne, Germany will speak about corneal vascularisation and Professor Peter Shah, UCL and Birmingham will speak about the diagnosis and management of neovascular glaucoma. Moving to the back of the eye, Miss Samira Anwar from Leicester will speak about retinopathy of prematurity, and then Miss Susan Downes, Oxford about age related macular degeneration and Miss Clare Bailey, University of Bristol proliferative diabetic retinopathy two of the most common causes of irreversible visual loss in the western world.

2.30pm: Corneal Vascularisation: Medical and Surgical Management *Professor Claus Cursiefen, Germany*

Prof. Dr. med. Claus Cursiefen undertook his medical studies at the Universities of Regensburg/Germany, Würzburg/Germany, King's College/London and University of Dundee/St. Andrews/Scotland, then his residence in the Department of Ophthalmology in Erlangen/Germany, under Prof. Naumann. He then completed a Postdoctoral Fellowship at the Schepens Eye Research Institute in Boston with Prof. Dr. Streilein and Prof. Dr. Dana.

Professor Cursiefen now splits his time between his research and clinical work. His clinical focus includes novel lamellar surgical techniques in corneal transplantation, cataract, glaucoma and refractive surgery as well as ocular surface reconstruction. His research focus is mechanisms of corneal hem- and lymphangiogenesis and their implications for corneal transplant immunology. He is also interested in modern lamellar corneal transplant surgery. He has more than 180 publications, amongst them publications in PNAS, JEM, JCI and Nature Medicine. Professor Cursiefen is involved in the editorial boards for important Ophthalmology journals including IOVS, Ophthalmologe and Klinische Monatsblätter fürAugenheilkunde. He has won several awards for his research and, in 2012 was awarded the "Achievement Award", American Academy of Ophthalmology (AAO). Professor Cursiefen is currently Chairman and Professor of the Department of Ophthalmology, University of Cologne, Germany since 2011 and an Adjunct Associate Scientist at Schepens Eye Research Institute/Harvard Medical School, Boston.

Corneal neovascularisation reduces corneal transparency and increases the risk of immune rejection after transplantation. Aim of the talk is to present current medical and surgical strategies to stop and regress pathologic corneal hem- and lymphangiogenesis.

2.55pm: Neovascular Glaucoma: Early diagnosis and Management *Professor Peter Shah, UCL and Birmingham*

Professor Peter Shah is a Consultant Ophthalmic Surgeon and Supra-Regional Glaucoma Specialist at University Hospitals Birmingham NHS Trust. He is also the Director of Education ("Eyes and Vision Theme") for University College London Partners and NIHR Biomedical Research Centre (Moorfields Eye Hospital and UCL Institute of Ophthalmology). He is Honorary Professor of Glaucoma at the Centre for Health and Social Care Improvement at the University of Wolverhampton. Prof Shah is an internationally-recognised leader in Glaucoma Surgery, and also specialises in Complex Cataract Surgery. He has written 6 Ophthalmology textbooks and has authored over 70 research publications. Professor Shah is a founder-member of the Midlands Glaucoma Society, past-chair of the British Eye Study Group, Secretary of the Council of the Oxford Ophthalmological Congress and a Council member of the British Ophthalmic Anaesthesia Society. As a teacher he has organised many national and international symposia and courses, including annual Glaucoma and Ocular Surface Disease Masterclasses , "Sailing A Safe Ship" (a leadership course for young

Consultants which focuses on patient safety and risk management), the Royal College Glaucoma Surgery Masterclass and the UCLP Trabeculectomy Wet-lab Academy. Professor Shah has a long-term interest in patient safety and risk management and is a national teacher in these areas. He is a past-Glaucoma section editor for "Eye" and is a reviewer for many international journals. Professor Shah is the leader of the "**ReGAE**" team – **Re**search into **G**laucoma **A**nd **E**thnicity – which aims to prevent avoidable glaucoma blindness in the diverse ethnic communities of the UK. He is also a member of a team of Eye Surgeons providing charitable support to an Ophthalmic Unit in Tanzania via "Sight for East Africa". Professor Shah has previously worked as Patron to the charity "Speight of the Art", which aims to seek out future artistic skills and talent in children from diverse backgrounds.

Professor Peter Shah will discuss techniques to enhance the early diagnosis and management of neovascular glaucoma. Emphasis will be on understanding the pathogenesis of the condition and the broad range of differential diagnoses. New treatment options will be considered in the light of existing management options.

3.50pm: Retinopathy of Prematurity: What to Look for and How to Treat *Miss Samira Anwar, University Hospitals Leicester*

This lecture aims to present a short overview of retinopathy of prematurity and why it is important. It will also cover the development of the retinal vasculature in order to understand the pathology and discuss clinical assessment. Finally there will be a presentation of a case highlighting the management in a difficult case of retinopathy of prematurity.

4.15pm: Wet Age Related Macular Degeneration: What's New? *Miss Susan Downes, Oxford University Hospitals*

Dr Susan Downes is a Consultant Ophthalmologist at the Oxford Eye Hospital and an Honorary Senior Lecturer in Clinical Ophthalmology at the University of Oxford, England. After graduating from Bristol University Medical School, and working overseas for a year in New Zealand, she was a resident on the Birmingham and Midland Eye Hospital rotation and then at Moorfields Eye Hospital and the Royal Berkshire Hospital. A post-residency fellowship in Medical Retina at Moorfields Eye Hospital followed, during which time she finished a higher degree (MD 2000) in inherited retinal degeneration at the Institute of Ophthalmology, UCL & London and Moorfields Eye Hospital. Dr Downes took up her Consultant position at the Oxford Eye Hospital in 2000, and is Lead for the Age Related Macular disease, and Retinal Genetics service. Her main research interests include inherited retinal dystrophies and macular disease. She is on the steering group for the UK trial investigating the use of Bevacizumab and Ranibizumab in the IVAN trial, and is PI and co-PI on a number of projects with wide ranging collaborations in retinal disease. Together with colleagues, she set up the United Kingdom Eye Genetics Group, and introduced the first NHS genetic testing for Stargardt disease in Oxford for the UK.

The lecture *"Exudative age related macular degeneration: What's new?"* aims to present the changing face of treatment provision for exudative AMD with reference to rapid access to the service, implementation of high volume treatment, and to discuss treatment options including evidence from IVAN, and potential future therapies.

4.40pm: Proliferative Diabetic Retinopathy: Is it History? *Miss Clare Bailey, University of Bristol*

Clare Bailey MD MRCP FRCOphth is a consultant ophthalmologist at Bristol Eye Hospital, specialising in medical retina disorders. She undertook a higher degree concerning diabetic retinopathy. She is actively involved in clinical research, particularly into diabetic retinopathy and age-related macular degeneration and leads the Retinal treatment and research unit at Bristol Eye Hospital.

In this presentation she will discuss the current research and treatment for diabetic retinopathy.

POSTER PRESENTATIONS

1 **Barriers to the Adoption of Regenerative Medicine Therapies in Ophthalmology**
James Rose, University of Nottingham

2 **Immunological Properties of Mesenchymal Stem Cells in Ophthalmology**
Matthew Branch, University of Nottingham

3 **The Role of Hepatocyte Growth Factor in Neovascular Age-Related Macular Degeneration: In Vitro Study of its Effect on Choroidal Endothelial Cells**
Govindi Jayanika Samaranayake, University of Nottingham

4 **Suitability of Endogenous Reference Genes for Gene Expression Studies with Human Intraocular Endothelial Cells**
Ruoxin Wei, University of Nottingham

5 **Augmented Vacuum-dried versus Cryopreserved Amniotic Membrane as an Alternative Ocular Surface Dressing**
Claire Allen, University of Nottingham

6 **Mother Nature's Bandage – Developments in the use of Amniotic Membrane in Ophthalmology**
Frederick Clough, Royal London Hospital

7 **Estimated UK Prevalence and Incidence of Late Age-related Macular Degeneration**
Zakariya Jarrar, University of London

8 **Comparative Profiling of Stem Cells Related Gene Networks and Pathways in the Limbal Epithelial Crypt with Ocular Surface Epithelial Regions**
Bina Kulkarni, University of Nottingham

9 **Alginate Hydrogels for Ocular Surface Repair using a Cornea Organ Culture Model**
Bernice Wright, University of Reading

10 **Characterisation of Cultured Stromal Cells: *In vitro* Restoration of the Keratocyte Phenotype using Co-culture Approaches**
Samantha Wilson, Keele University

11 **Regulation of Genotype and Phenotype of Corneal Stromal Cells**
Samantha Wilson, Keele Uinversity

12 **Optimisation of a Lagomorph *in vivo* Corneal Deepithelialisation Model**
Owen M^{c}Intosh, University of Nottingham

13 **Cultivation and Characterization of Corneal Limbal Epithelial Stem Cells on Lens Capsule in Animal Material-free Medium**
Réka Albert, Department of Ophthalmology, University of Debrecen, Hungary

14 **Analysis of Visual Fixation Patterns Preceding the Selection of a New Preferred Retinal Locus used in Low Vision Rehabilitation with Microperimetry**
Marco Morales, Nottingham University Hospitals

15 **Corneal Nerves In The Laser In-Situ Keratomileusis (LASIK) Treated Cornea**
Lana Faraj, University of Nottingham

POSTER PRESENTATION ABSTRACTS

The Poster Exhibition is located in the Main Conference Hall

1: Barriers to the Adoption of Regenerative Medicine Therapies in Ophthalmology

James Rose, Alicia El Haj, Felicity Rose, Andrew Hopkinson, David Williams

University of Nottingham

Introduction: Adoption and reimbursement of regenerative medicine products in general is relatively unchartered territory, with very few technology demonstrators making it to the market. However understanding the processes involved in the uptake of these therapies into healthcare will be critical to the creation of a viable and sustainable regenerative medicine industry sector. Using Ophthalmology as a demonstrator clinical area, this work gauges the perceptions of a wide range of stakeholders involved in the adoption process in both the UK and Canada. The mixed methods approach makes qualitative and quantitative

assessments of the most significant barriers to adoption and subsequent diffusion of novel health technologies in this area.
Results: The use of problem-centred interviews yielded was interpreted through use of open coding. Several key themes emerged from interpretation of the interviews; these included the idea that there are several levels of concern in this complex process, involving features of the technology, features of typical customers, and the organisational structure of both care delivery but also budget management at the micro and macro level. These ideas were supported with a section of surveys, supporting the idea that these barriers are indeed important.
Conclusions: This work demonstrates that in healthcare systems such as Canada and the UK which notably single-payer systems, blunt policy instruments have at current little effect on the adoption and diffusion of novel healthcare technologies. Emerging regenerative medicine therapies in ophthalmology at current are relatively unproven against the long- term promises of cost savings and efficacy. It is likely that demonstrations of the cost utility of these therapies will come in the favoured US market. Single payer healthcare systems will require this evidence base to invest in these typically costly therapies.

2: Immunological Properties of Mesenchymal Stem Cells in Ophthalmology

Branch MJ, McIntosh O, Dua HS and Hopkinson A.

Division of Ophthalmology and Visual Sciences, University of Nottingham.

Introduction: There are chronic transplant shortages for many tissues including the cornea. Reducing this deficit is the focus of significant clinical research. Allogeneic transplantation requires HLA matching and to compound these issues, immune rejection of matched tissues may still occur. Autologous material is used when possible however bilateral corneal disease necessitates the use of allogeneic material. Regenerative medicine approaches use stem cells to regenerate lost or damaged tissue where there are currently insufficient donor supplies.
MSC have been shown to enhance corneal wound healing in model systems. MSC are found within the corneal stroma and are thus likely to be crucial to its function and maintenance. Mesenchymal stem cells (MSC) are reportedly non-immunogenic however variations between different sources and preparations of MSC are known to possess variable immunological properties.
Methods: Fetal liver MSC (flMSC) were incubated with peripheral blood mononuclear cells (PBMC) labeled with fluorescent 5(6)-CFDA, SE; CFSE. Immunogenic stimulation of the $CD3^+$ lymphocytes within PBMC causes proliferation which was indicated by a reduction in fluorescence. Lymphocytes were stimulated with γPBMC from a different donor or phytohemagglutinin as a control along with unlabeled and labeled unstimulated controls. TNFα and IFNγ were used separately and in combination to simulate inflammatory conditions which may promote flMSC immunogenicity. Mixed lymphocyte reactions were also used to assess the ability of flMSC to modulate the local immune response
Results: FlMSC did not elicit a reaction from lymphocytes and were able to suppress their stimulation even in the presence of third party antigens. Lymphocyte stimulation with mitogens and inflammatory cytokines in the presence of flMSC did cause some proliferation however this was reduced compared to stimulated controls without flMSC.
Conclusions: This provides evidence which suggests flMSC may reduce the likelihood of rejection for allogeneic transplantation. However there is still a risk flMSC may be immunogenic within the complex and inflammatory conditions present in transplantation which may precipitate into transplant rejection.

3: The Role of Hepatocyte Growth Factor in Neovascular Age-Related Macular Degeneration: In Vitro Study of its Effect on Choroidal Endothelial Cells

Govindi Jayanika Samaranayake, Elizabeth Stewart, Winfried Amoaku

Division of Ophthalmology and Visual Sciences, University of Nottingham

Introduction: Intraocular angiogenesis is associated with a number of common blinding conditions including neovascular age-related macular degeneration (nAMD). The growth factor, vascular endothelial growth factor (VEGF) is reported as being central in driving choroidal neovascularisation (CNV) in nAMD. For this reason, contemporary clinical therapies of nAMD involve targeting VEGF with intravitreal anti-VEGF drugs e.g.

ranibizumab and bevacizumab. However, these have limited success and require repeated treatments for prolonged periods. Other cytokines are known to be involved in CNV development including hepatocyte growth factor (HGF), which has been shown to have a role in the early stages of nAMD. Most research relating to HGF and its receptor c-met have been reported in tumour cells. Our aim was to elucidate the effects of HGF on primary human choroidal endothelial cells (hCEC), and investigate co-operation with VEGF.
Methods: hCEC were isolated, cultured and characterised. The expression of c-met and associated molecules in hCEC was detected using western blotting, immunofluorescence, flow cytometry and qPCR. Proliferation and other angiogenesis assays were used to assess and compare the effects of HGF and VEGF on hCEC.
Results: Expression of endothelial markers and the growth factor receptors c-met, VEGFR2 were found in both whole choroid sections and cultured cells. HGF was found to have a similar effect on hCEC proliferation and angiogenesis as VEGF. These effects were additive, an indication of the co-operative signalling which occurs between these molecules.
Conclusions: A more efficient approach to regulate intraocular angiogenesis would aim to simultaneously block the actions of multiple growth factors, or the common downstream site in the angiogenesis pathway. This project provides insight into the interactions or cross-talk in human choroidal endothelial cell signalling. Future targeting of multiple growth factors may provide a more sustained treatment response in order to enhance treatment protocols in nAMD.

4: Suitability of Endogenous Reference Genes for Gene Expression Studies with Human Intraocular Endothelial Cells

Ruoxin Wei, Elizabeth Anne Stewart and Winfried M Amoaku

Division of Ophthalmology and Visual Sciences, University of Nottingham

Background: The use of quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR) has become widely applied as a method to measure transcript abundance. In order to be reflective of biological processes during health and disease this method is dependent on normalisation of data against stable endogenous controls. However, these genes can vary in their stability in different cell types. The importance of reference gene validation for a particular cell type is now well recognised and is an important step in any gene expression study.
Results: Cultured primary human choroidal and retinal endothelial cells were treated with the immunostimulant polyinosinic: polycytidylic acid or untreated. qRT-PCR was used to quantify the expression levels of 10 commonly used endogenous control genes, *TBP*, *HPRT1*, *GAPDH*, *GUSB*, *PPIA*, *RPLP0*, *B2M*, *18S rRNA*, *PGK1* and *ACTB*. Three different mathematical algorithms, GeNorm, NormFinder, and BestKeeper were used to analyse gene stability to give the most representative validation. In choroidal endothelial cells the most stable genes were ranked as *HPRT1* and *GUSB* by GeNorm and NormFinder and *HPRT1* and *PPIA* by BestKeeper. In retinal endothelial cells the most stable genes ranked were *TBP* and *PGK1* by GeNorm and NormFinder and *HPRT1* by BestKeeper. The least stable gene for both cell types was *18S* with all 3 algorithms.
Conclusions: We have identified the most stable endogenous control genes in intraocular endothelial cells. It is suggested future qRT-PCR studies using these cells would benefit from adopting the genes identified in this study as the most appropriate endogenous control genes.

5: Augmented Vacuum-dried versus Cryopreserved Amniotic Membrane as an Alternative Ocular Surface Dressing

CL Allen, G Clare, OD M^{c}Intosh, H Dua, A Hopkinson

Division of Ophthalmology and Visual Sciences, University of Nottingham

Introduction: Differences in amniotic membrane (AM) preservation techniques can significantly influence bio-chemical and mechanical properties, reducing clinical efficacy. This study was established to investigate the effects of vacuum-drying in the absence and presence of saccharide lyoprotectants, compared to standard cryopreservation techniques.
Methods: AM was cryopreserved (CPAM) or vacuum-dried (VDAM) with and without treatment with D-(+)-Trehalose dihydrate (VDAM/EGCG/Tre) or D-(+)-Raffinose pentahydrate (VDAM/EGCG/Raff) and the antioxidant epigallocatechin (EGCG). Structural and visual comparisons were assessed using EM. AM

biochemical factor profiles and stability were compiled and assessed using immunoassays. Factor localisation and expression were determined using immunofluorescence. AM biocompatibility with primary corneal epithelial and keratocyte cell populations were assessed using standard cell proliferation, cytotoxicity, apoptosis and migration assays. Inflammatory factor modulation of AM was analysed using cytometric beads and flow cytometry.
Results: Structural assessment showed that vacuum-drying devitalises AM epithelium, but less so than cryopreservation and the extent of damage is reduced when pre-treated with saccharide. VDAM alone and VDAM/EGCG/Tre and VDAM/EGCG/Raff showed greater factor retention efficiencies and bioavailability compared to CPAM and demonstrated a more sustained biochemical factor time release *in vitro*. Cellular health assays showed that VDAM and VDAM/Tre/Raff are compatible and superior substrates for primary CEC expansion. Wound healing assays additionally showed a significant increase in epithelial wound closure rate when cultured with VDAM/EGCG/Raff, compared to CPAM and control.
Conclusions: This study has shown that our optimised vacuum-dried AM product is a superior substrate to conventionally cryopreserved AM with enhanced bio- chemical and mechanical properties, increasing its clinical efficacy.

6: Mother Nature's Bandage – Developments in the use of Amniotic Membrane in Ophthalmology

Frederick Clough, Alexander Ferdi, Nish bedi

Royal London Hospital, Royal Free Hospital & Queen Elizabeth Hospital Birmingham

Purpose: Amniotic membrane (AM) has been used in surgical procedures in ophthalmology since the 1940's. Its benefits relate to its ability to promote epithelialization while suppressing scarring, angiogenesis and stroma proliferation. It's true clinical potential, however, is not completely understood.
Methods: Since the early 1990's the breadth of indications for which it is currently used in ophthalmology has been widening, in particular as a first alternative to existing management options. This review will focus on the recent advances in this field and lay out some of the potential uses comparing amniotic membrane to other synthetic alternatives.
Results: Recent work in this field focuses on the suggestions for a single, unifying membranous component responsible for the properties of AM, and to identify the potential of AM as a scaffold network for extracellular culture of autologous transplants for treatment of ocular surface disorders.
Conclusions: Our findings show AM as a superior therapeutic method to synthetic alternatives in its role as a biological pansement, and that the scope of indications for its use may be wider than current practices.

7: Estimated UK Prevalence and Incidence of Late Age-related Macular Degeneration

Zakariya Jarrar,[1] Christopher Owen,[1] Richard Wormald,[2,3] Derek Cook,[1] Astrid Fletcher,[2] Alicja Rudnicka[1]

[1]St.George's, University of London, [2]London School of Hygiene & Tropical Medicine, [3]Moorfields Eye Hospital, London

Purpose: UK estimates of age-related macular degeneration (AMD) occurrence vary. This study aims to estimate prevalence, number and incidence of late AMD by type in the UK population aged >50 years.
Methods: Age-specific prevalence rates of AMD obtained from a Bayesian meta-analysis of AMD prevalence were applied to UK 2007-2009 population data. Incidence was estimated from modelled age-specific prevalence.
Results: Overall prevalence of late AMD was 2.4% (95% credible interval (CrI) 1.7% to 3.3%), equivalent to 513,000 cases (95% CrI 363,000 to 699,000); estimated to increase to 679,000 cases by 2020. Prevalence rates of geographical atrophy (GA) and neovascular AMD (NVAMD) were 1.3% (95% CrI 0.9% to 1.9%) and 1.2% (95% CrI 0.9% to 1.7%), respectively. Estimated number of prevalent cases of late AMD was 60% higher in women (314,000 cases) versus men (192,000 cases). Number of new cases per year of late AMD, GA and NVAMD in women was 45,000 (95% CrI 26,000 to 77,000), 27,000 (95% CrI 16,000 to 44,000) and 26,000 (95% CrI 15,000 to 45,000); in men 25,000 (95% CrI 14,000 to 43,000), 16,000 (95% CrI 10,000 to 27,000) and 13,000 (95% CrI 7,000 to 23,000), respectively. A total of 44,000, 40,000 and 71,000 new cases of GA, NVAMD and late AMD were estimated per year, respectively.

Conclusions: This study estimates the prevalence and incidence rates of AMD by type. These estimates are more accurate than previous estimates and will help guide health and social service provision for those with late AMD and enable estimation of the cost of introducing new treatments.

This work was funded by the Macular Disease Society

8: Comparative Profiling of Stem Cells Related Gene Networks and Pathways in the Limbal Epithelial Crypt with Ocular Surface Epithelial Regions

Bina Kulkarni, Andrew Hopkinson, Harminder S Dua.

Division of Ophthalmology and Visual Sciences, University of Nottingham

Purpose: Comparative transcriptional profiling of ocular surface (OS) epithelial regions such as cornea, Limbal Epithelial Crypt (LEC) and limbus was performed with Gene ST 1.0 array, to identify the biology of these ocular surfaces (OS) regions with emphasis on identification of stem cell (SC) properties of LEC.
Methods: Lasermicrodissected RNA samples from the LEC, limbus and corneal epithelium were hybridised to Gene 1.0 ST array chips. The raw microarray data was normalised and imported to Qlucore software. Differentially expressed gene list for each OS regions was analysed with GeneGo and Ingenuity Pathway Analysis to determine pathways and geneontology of interest.
Results: Comparison of transcription factors gene networks, pathways and geneontology revealed that LEC was enriched for up regulated gene functions expressed in quiescent SCs, developmental processes and SC pathways. Interestingly, LEC was also enriched for acute phase response signalling indicating a crucial role of LEC during corneal wound healing and immunity. On the other hand, cornea and limbus were enriched for GO terms and pathways related to proliferating SC (PSC), transient amplifying cells (TAC) and differentiated cells (DC). Cornea was also enriched for cell cycling, self-renewal genes.
Conclusions: This study demonstrates that LEC is a reservoir of QSC, which are activated in the event of corneal epithelial stress or OS wounding. The findings in this study provide molecular evidence for the presence of PSCs or "transient cells" in the cornea, supporting the recently published evidence that the cornea is capable of maintaining its epithelial regeneration in normal OS health conditions.

9: Alginate Hydrogels for Ocular Surface Repair using a Cornea Organ Culture Model

Bernice Wright, Shengli Mi, Bo Chen, Vitaliy Khutoryanskiy and Che J. Connon

Stem cells and nanomaterials laboratory, Reading School of Pharmacy, University of Reading

Purpose: Therapy for limbal stem cell deficiency, a leading cause of corneal blindness, may be improved by application of therapeutic cells and drugs which promote corneal epithelialisation using biocompatible hydrogels for their delivery. The present study aims to investigate alginate hydrogels as ocular bandages for the delivery of LEC and ophthalmic drugs for repair of the wounded ocular surface.
Methods: The entire cornea was excised from the eye (bovine model) and suspended on an agar and medium support. Alginate gel discs were formed with or without the live cell porogen, hydroxy ethyl cellulose (HEC), and 102 mM $CaCl_2$ was used for gelation. A 7mm diameter area of the central cornea was de-epithelialised, and 1.2% (w/v) alginate gel discs with or without (untreated control) Y27632 (100 μM) and gels containing LEC were placed over wounded corneas for 3 days. Treated corneas were embedded in TissueTek, cryosectioned and stained with haematoxylin and eosin. Cell viability was assessed by Trypan blue exclusion and LEC differentiation was investigated using Western blotting.
Results: LEC were robustly viable in alginate gels discs and a population of these cells remained in an undifferentiated state, suggesting the presence of progenitor LEC. Cell viability was significantly enhanced with increases in internal pore size mediated by HEC. Although LEC were viable within alginate gels for the duration of the treatment period and successfully delivered to damaged corneas, these cells did not induce epithelialisation of the cornea. Y27632 delivered using unmodified alginate gels (1.2% (w/v)) did not induce corneal repair, but HEC-modified alginate gels may allow more efficient diffusion of this drug to the corneal surface.

Conclusions: Alginate gel discs with modified internal porosity may be used as delivery agents for ocular surface repair. These hydrogels may be used as ocular bandages for the controlled release of ophthalmic drugs.

10: Characterisation of Cultured Stromal Cells: *In vitro* Restoration of the Keratocyte Phenotype using Co-culture Approaches

Samantha L Wilson, Ying Yang and Alicia J. El Haj

Institute for Science and Technology in Medicine, School of Medicine, Keele University

Purpose: *In vivo,* epithelial cells are in close contact with keratocytes[1, 2] in the stromal layer; they are connected both anatomically and functionally[3] and it is these interactions that are vital to the maintenance of tissue homeostasis and transparency. Co-culture studies aim to recapture this cellular anatomy and functionality by bringing together two or more cell types within the same culture environment, enabling them to interact and communicate. By more closely mimicking the *in vivo* cellular niche environment we are able to aid our understanding of corneal wound healing mechanisms and the importance of cell mediated interactions; thus enabling us to engineer corneal tissue with stromal cells that are in a healthy, native, uninjured state.
Methods: Three different co-culture methods have been examined; epithelial direct explant; transwell; the use of conditioned media and their effects on stromal cell function were studied. The different co-culture models help us to determine as to whether cell-cell interactions are due to direct cell contact or not, and as to whether the cells themselves have to be present to elicit a response.
Results: We have demonstrated that it is possible to revert cultured corneal stromal cells that are fibroblastic in lineage towards the native uninjured cell type in terms of cell behaviour and biological properties.
Conclusion: This method of activating corneal keratocytes into their fibroblastic lineage and then being able to differentiate them back to the keratocyte lineage is vital to corneal tissue engineering with its benefits being threefold; firstly, it allows for sufficient numbers of corneal stromal cells to be grown up quickly and easily in serum-containing media; secondly the ability to differentiate the expanded activated cells back to a keratocyte linage is important in aiding our understanding of corneal wound healing mechanisms and the importance of the cell interactions during these processes; and finally it allows us to engineer corneal tissues that more closely mimic the native cornea, with cells that are in a healthy uninjured state which may have the potential to act as an important tool in with regards to toxicity testing of drugs and irritants which could in turn improve the development of new and improved ocular drugs to treat corneal disease and/or injury.

11: Regulation of Genotype and Phenotype of Corneal Stromal Cells

Samantha L. Wilson[1], Ian Wimpenny[1], Mark Ahearne[1,2], Saaeha Rauz[3], Alicia J. El Haj[1], Ying Yang[1]

[1]Institute for Science and Technology in Medicine, School of Medicine, Keele Uinversity, [2]Trinity Centre for Bioengineering, Trinity College Dublin, Dublin, [3]Academic Unit of Ophthalmology, School of Immunity and Infection, University of Birmingham

Purpose: Control and maintenance of keratocyte phenotype is vital to developing *in vitro* tissue engineered strategies for corneal repair. In this study the influence of topographical and chemical cues on mechanical, phenotypical and genotypical behaviour of adult human derived corneal stromal (AHDCS) cells in three dimensional (3D) constructs are examined.
Methods: Topographical cues are provided *via* multiple aligned electrospun nanofibre meshes which are capable of aligning individual cells. Chemical cues are examined using different media supplementation. A non-destructive indentation technique and optical coherence tomography are used to determine the elastic modulus and dimensional changes, respectively. qPCR analysis revealed that the shift between keratocyte and fibroblast marker expression could be adjusted by both chemical and topographical factors.
Results: Changing the surrounding niche from 2D (TCP) to 3D (collagen hydrogel) conditions in serum-containing media increased keratocyte marker gene expression and decreased fibroblast marker expression which was further enhanced by removal of serum, media supplements and the presence of orientated nanofibers. Cells cultured on aligned nanofibres were more elongated, organised and orientated compared to the random orientation of cells grown in fibre-free constructs. There was a correlation between elastic

modulus, contractile characteristics and gene expression. Constructs containing nanofibres have a higher initial modulus, reduced contraction and organised cell orientation compared to those without nanofibres. Cell-seeded constructs cultured in serum-containing media increased in modulus throughout the culture period and underwent significantly more contraction than constructs cultured in serum-free and insulin-containing media. This implies that the growth factors present in serum promote a fibroblast-like phenotype; qPCR data further validates these observations.
Conclusion: The results from these studies indicate that the synergistic effect of nanofibres and serum-free media plus insulin supplementation in a 3D collagen culture environment provide the most suitable environmental, topographical and chemical niche for reverting cultured AHDCS cells to a native keratocyte lineage. The combination of non-destructive monitoring techniques and analysis of gene expression provide important feedback for optimizing culture condition, which has not previously been shown in 3D corneal models.

12: Optimisation of a Lagomorph *in vivo* Corneal Deepithelialisation Model

Owen Douglas M[c]Intosh, Dr Claire Louise Allen, Dr Andrew Hopkinson, Professor Harminder Singh Dua

Division of Ophthalmology and Visual Sciences, University of Nottingham

Introduction: The rabbit ocular surface (OS) has been used for many years as a reliable comparison to study human corneal injuries. The aim of this work was to create a standardised corneal epithelial surface injury using an alkali insult. For reliable *in vivo* data to be collected the area of effects of the deepithelialisation must be optimised and repeatable. We would then use this model to test ocular bandages and substrates.
Methods: Eyes were enucleated from New Zealand White rabbits and stored in Dulbecco's phosphate buffered saline (DPBS) with antibiotics. The central cornea was deepithelialised with sodium hydroxide (NaOH) solution using a range of concentrations (0.3N – 4N) and duration (30 seconds – 15 minutes) using a corneal zone marker.. Corneal discs were dissected from the whole eye, and the injuries assessed using haematoxylin and eosin staining and transmission electron microscopy (TEM).
Results: Microscopy showed that the higher concentrations of NaOH and extended durations caused irreversible damage to the cornea, with the removal of the epithelial layer and deep structural damage to the stroma. The degree of damage correlated with both concentration and duration.
Conclusion: The optimisation process showed that 0.3N NaOH for 30 seconds was sufficient to deepithelialise the cornea without causing stromal damage and creating an injury that would respond and heal with treatment. This model is now in use, testing the biocompatibility and efficacy of various ocular surface treatment substrates.

13: Cultivation and Characterization of Corneal Limbal Epithelial Stem Cells on Lens Capsule in Animal Material-free Medium

Réka Albert [1,2], Zoltán Veréb[3*], Krisztián Csomós[2], Morten C Moe[4], Erik O Johnsen[4], Ole Kristoffer Olstad[5], Bjørn Nicolaissen[4], Éva Rajnavölgyi[3], László Fésüs[2], András Berta[1], Goran Petrovski[1,2]*

[1]Department of Ophthalmology, [2]Stem Cells and Eye Research Laboratory, Department of Biochemistry and Molecular Biology and [3]Department of Immunology, University of Debrecen, Medical and Health Science Center, Debrecen, Hungary; [4]Centre of Eye Research, Department of Ophthalmology, and [5]Department of Medical Biochemistry, Oslo University Hospital and University of Oslo, Oslo, Norway [*]Authors contributed equally

Purpose: To develop a simple, reproducible and animal-material free method for cultivating and differentiating human limbal stem cells (LSCs) into corneal epithelium on human lens capsule (LC), for clinical transplantation.
Methods: Limbal rims were harvested from cadavers with the permission of the Regional Ethical Committee and expanded ex vivo on either cell culture plates or LC, in medium containing human serum as the only growth supplement. Cell viability was measured by MTT and Annexin-V/Propidium iodide assays and cells were characterized by genome-wide microarray analysis, immunocytochemistry and flow cytometry.
Results: The cell viability of the outgrowing cells was >97% within two weeks of cultivation and the percentage of early and late apoptotic cells remained low accordingly. Transcriptional profiling of LESCs indicated a

relatively high transcriptional difference compared to differentiated corneal epithelial cells, including genes involved in ion-, nucleotide –or protein binding, as well as receptor or enzyme activities. Immunostaining revealed the non-hematopoetic, -endothelial and –mesenchymal stem cell phenotype of LESCs, while cell adhesion molecules, integrins and lectin-based surface carbohydrate profiling showed a specific pattern on these cells.
Conclusion: We report a novel method combining the use of medium with human serum as the only growth supplement with LC for cultivating, characterizing and expanding cornea LESCs from cadavers for possible treatment of LESC deficiency.

14: Analysis of Visual Fixation Patterns Preceding the Selection of a New Preferred Retinal Locus Used in Low Vision Rehabilitation with Microperimetry

Marco U Morales, Saker Saker, Rajnikant L Mehta, Martin Rubinstein, Winfried Amoaku

Department of Ophthalmology, Queen's Medical Centre, Nottingham University Hospitals, Nottingham, UK

Background and aims:
Patients with pathologies such as age-related macular degeneration (AMD) affecting the central part of the retina may lose their central vision ability altering fixation capabilities.
The rehabilitation of eccentric and unstable vision can be improved by training a new selected retinal locus with better functional characteristics using Microperimetry systems with Biofeedback technology.
The Microperimetry system MAIA (Centervue, Padova Italy), produces estimates of preferred retinal locus (PRL) during the initial 10 seconds of testing (PRL_High), as well as for the entire test time (PRL_Low). The aim of this study was to analyse both fixation loci PRL_H and PRL_L preceding the subjective selection of a new Retinal Locus for eccentric vision training.
Materials and methods: 41 patients, with different diagnosed retinal pathologies, were assessed for fixation characteristics. Each underwent a microperimetry exam with the central 10° and 37 points grid which lasts about 6 minutes. Patients were asked to concentrate their vision on the fixation target (1 degree diameter circle) during the whole exam time. PRL_High (H) is calculated when patients dedicate their highest fixation attention during the first 10 seconds of testing with no interference from microperimetric stimuli projection. The PRL_Low (L) is calculated at the end of the exam from all data available. Automatic estimates of fixation stability (stable, relatively unstable, unstable) are produced by the instrument based on all available data for the test.
Results: 46 eyes were categorized as stable fixation, 8 as relatively stable and 11 as unstable. All 11 eyes with unstable fixation and 7 eyes with relatively unstable fixation were found to have their PRL_H and PRL_L in different position with a separation distance from 0.5° to 5° (mean distance = 2.27°, SD = 1.43°). 1 eye with relatively unstable fixation had the PRL_H and PRL_L in the same position, which was the anatomical fovea. 2 eyes with stable fixation had their PRL_H and PRL_L in different position with a separation distance of 0.5° and 1.2°, although in both cases the PRL_L was located inferior from the fovea.
1 eye with unstable fixation had the PRL_H and PRL_L located in the same position 5° superior-nasal from the fovea.
Conclusions: Patients with central and stable fixation have their PRL_H and PRL_L in the same anatomical position which is located over the foveal area showing uniform fixation stability. However, patients, with unstable and relatively unstable fixation may use different retinal zones to fixate during longer task periods. The PRL_H and PRL_L estimates can be used for more precise assessment of fixation stability in two steps during the same fixation attempt. The location of both PRL_H and PRL_L may be considered when selecting a new PRL during the eccentric vision training for better rehabilitation outcomes.

15: Corneal Nerves In The Laser In-Situ Keratomileusis (LASIK) Treated Cornea

Lana A Faraj, Virinder K Dhillon, Harminder S Dua

Division of Ophthalmology & Visual Sciences, Queens Medical Centre, University of Nottingham

Purpose: We aimed to provide histological evidence of the morphology and architecture of regenerated corneal nerves in 2 LASIK treated corneas.

Methods: 2 whole corneas from a 41 year old deceased male who had previous LASIK surgery were used in this study. Both corneas were stained as whole mounts using the Karnovsky & Roots direct coloring thiocholine modification of AChE technique. Each specimen was scanned enface using the Hamamatsu Nanazoomer digital pathology microscope.
Results: All types of nerves were seen to be present in both corneas. Fewer stromal nerves were seen to enter the cornea peripherally. Perforation sites, from which the sub-basal nerves arise in normal corneas, were also seen to be present within the LASIK treated zone.
Several morphological abnormalities were noted within the treatment zone including twisting, coiling, abnormal branching and increased stromal nerve tortuosity. Fine nerves or sprouts and excresences were seen arising along thicker stromal nerves. Also, the central clockwise whorl of the central sub-basal nerves were absent in both corneas, in keeping with some previous studies using in-vivo confocal microscopy (IVCM).
Conclusion: Dry eye remains the single most common complication after LASIK surgery, even with successful visual outcomes. Similar abnormalities have also been noted in patients with dry eye using IVCM. These changes are thought to occur as a result of the high metabolic nature of the regenerating nerves, occasionally leading to the misdirected growth seen. The presence of perforation sites might suggest that these structures may in fact regenerate after surgery.

PREVIOUS PRIZE WINNERS

NOTTINGHAM RESEARCH TROPHY

A rolling trophy and an individual shield awarded to the best presentation in the clinical research category considered by a panel of judges on the day.

2012: G Maconachie, University of Leicester. *Effect of Compliance to Glasses Wear on Outcome of Visual Acuity After Refractive Adaptation*

2011: M G Thomas, University of Leicester. *High Resolution in-vivo Imaging in Achromaptosia*

2010: M Al-Aqaba, University of Nottingham. *Architecture and Distribution of Human Corneal Nerves*

2009: M G Thomas, University of Leicester. *Voluntary Modulation of Involuntary Eye Movements During Reading*

2008: A Bhan-Bhargava, University of Nottingham. *Glaucoma in an Elderly Caucasian Population (The Bridlington Eye Assessment Project)*

2007: A Shwe-Tin. *Digital Infrared Pupillometry for Comparing Cocaine with Apraclonidine Testing when Investigating Horner's Syndrome*

2006: M J Hawker. *Linear Regression Modelling of Rim Area to Discriminate Between Normal and Glaucomatous Optic Nerve Heads: The Bridlington Eye Assessment Project*

2005: M Awan, University of Leicester. *Can Patching be Improved in Amblyopia Treatment?*

2004: V S Maharajan, University of Nottingham. *Amniotic Membrane Transplantation for Ocular Surface Reconstruction: A Seven Year Retrospective Analysis*

2003: M Awan, University of Leicester. *Effect and Compliance of Strabismic Amblyopia Monitored with the Occlusion Dose Monitor*

2002: D Squirrell. *A Prospective, Case Controlled Study of the Natural History of Diabetic Retinopathy and Maculopathy after Uncomplicated Phacoemulsification Cataract Surgery in Patients with Type 2 Diabetes*

2001: J Morgan, University of Nottingham. *The Detection of T-Cell Activation by Retinal Autoantigen in Uveitis Patients using Cytokine Flow Cytometry*

2000: C Weir. *Spatial Localisation in Esotropia - is Extraocular Muscle Proprioception Involved?*

1999: P Hossain. *A Method to Visualise Leukocytes in the Retinal and Choroidal Circulation in vivo*

1998: C M Sloper, University of Nottingham. *Tacrolimus in High-Risk Corneal and Limbal Transplants*

1997: A R Sarhan, University of Nottingham. *Rapid Suture Management of Post-Keratoplasty Astigmatism*

DAVID MEYER RESEARCH TROPHY

A rolling plaque and an individual shield awarded to the best presentation in the basic science research category considered by a panel of judges on the day.

2012: K Hashmani, University of Nottingham. *Corneal Stromal Stem Cells – A Mesenchymal Epithelial Transition*

2011: P Dhillon, University of Nottingham. *Characterisation of Corneal Stromal Cells as a Novel Mesenchymal Stem Cell Source*

2010: M G Thomas, University of Leicester. *High Resolution Spatial and Temporal Expression Profile of FRMD7 in Neuronal Tissue Provides Clues for Pathogenesis and Treatment*

2009: I Mohammed, University of Nottingham. *Interleukin-1 Beta induced RNase-7 Expression requires MAPK but not NF-kB Signalling*

2008: E A Stewart, University of Nottingham. *Human Choroidal Endothelial Cell Growth Factor Signalling in Age-Related Macular Degeneration*

2007: S Thomas, University of Leicester. *Mutations in FRMD7, a Novel Gene, Cause X-linked Congenital Idiopathic Nystagmus*

2006: A Hopkinson, University of Nottingham. *Amniotic Membrane for Ocular Surface Reconstruction: Donor Variations and Handling affect Membrane Constituents*

2005: K H Weed. *In vivo Confocal Microscopy: Corneal Changes Following Retinal Detachment Surgery with Intra-ocular Silicone Oil*

2004: A Browning, University of Nottingham. *The Isolation and Characterisation of Adult Human Sub-macular Inner Choroidal Endothelial Cells*

2003: R D Hamilton, University of Nottingham. *Characterisation of an In vitro Model for Studies into Age Related Macular Degeneration*

NOTTINGHAM POSTER PRIZE

An individual shield awarded to the best poster presentation considered by a panel of judges on the day.

2012: M Branch, University of Nottingham. *Lymphocyte Proliferation Assay for Ophthalmology based Tissue Engineering*

2011: U Fares, University of Nottingham. *Correlation of Central and Peripheral Corneal Thickness in Healthy Corneas*

2010: I Mohammed, University of Nottingham. *Human Defensin 9, a 'Functional' Host Defence Protein*

2009: A M Otri, University of Nottingham. *Expression Pattern of Anti-microbial peptides (AMPs) in Acanthamoeba Keratitis*

2008: M Mathew, University of Nottingham. *Malignancies after Tacrolimus Therapy in the Management of Ocular Inflammatory Disease*

2007: J-J Gicquel, Poitiers, France. *A 24-month Follow-up of Severe Ocular Burns with Impression Cytology*

2006: P Ji. *Retinal Features in Children with Down's Syndrome*

2005: H Kolli. *Intravitreal Triamcinolone Acetonide in the Management of Refractory Uveitis*

2004: I Choudhari, University of Leicester. *National Survey of Management of Acquired Nystagmus*

2003: P Tesha, University of Leicester. *Interactive Teaching in Ophthalmology*

2002: D Thomas. *The Taut Thickened Posterior Hyaloid (TTPH)*

2001: R Amankwah, University of Nottingham. *Hyaluronic Acid Promotes the Migration of Corneal Epithelial Cells In vitro*

2000: I A El-Ghrably, University of Nottingham. *Quantitative Assessment of Cytokine mRNA and Secreted Protein in Proliferative Vitreoretinopathy*

1999: A Pearson. *Does Ethnic Origin Influence the Incidence or Severity of Keratoconus?*

1998: R Ahmed, University of Nottingham. *Modified Sheridan Gardiner Vision Test with Semi-transparent Card*

1997: D Raj, University Hospitals Nottingham. *Stem Cell Deficiency of the Corneosleral Limbus: a New Approach to Surgical Management*

HONORARY DELEGATES

Nomination of delegates as "Honorary delegates" of the Symposium was considered for the first time in 2006. This was to recognise individuals who had supported the meeting and contributed to it over the years. These delegates have the privilege of full participation and attendance in the meeting as guests of the Symposium.

Mr Nicholas R Galloway, Nottingham (2006)

Professor Larry Donoso, Wills Eye Hospital, Philadelphia (2010)

Mr A A Zaidi, Rotherham, UK (2011)

Professor Martin Rubinstein, UK (2012)

NEXT MEETING

The 18th Nottingham Eye Symposium and Research Meeting
***featuring the Norman Galloway Lecture* will be held on**
Friday, 31st January 2014 (provisional date)

- *Research trainee abstract presentations (oral and poster) and prizes*
- *Guest presentations by leading optometrists*
- *A symposium with talks from prestigious ophthalmologists*
- *The Norman Galloway Lecture*
- *Excellent conference facilities including free parking*
- *Tea, coffee and a hot buffet lunch provided*
- *All for a very reasonable registration fee!*

Contact the NES Meeting Co-ordinator: nes@nottingham.ac.uk to receive details on the next meeting and check out the website for details of previous and next year's meetings.
http://www.nottingham.ac.uk/scs/divisions/ophthalmologyvisualsciences/nes/index.aspx

For the latest news on the Eye Symposium
Follow us on twitter: twitter.com/eyesymposium
Like us on facebook: www.facebook.com/eyesymposium
and join us on linkedin: www.linkedin.com/groups/Nottingham-Eye-Symposium-3806753/about?trk=anet_ug_grppro

Also coming soon, our new Nottingham Centre for Eye Research (NCER) website, www.ncer.co.uk this will be a hub for ophthalmology research, clinical, and educational material as well as information relating to our up and coming commercial ophthalmic products

We make it visible.

We would like to take this opportunity to thank these organisations for their kind support and sponsorship of this event