

OCT images and could help to a better understanding of retinal diseases diagnosis and progression.

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### Structural biomarkers in neurodegeneration

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**Summary:** The aim of this study is to compare macular retinal layers and choroidal thicknesses of patients with Alzheimer's disease (AD) with those of patients without other known ophthalmological pathology, using spectral domain optical coherence tomography (SD-OCT). Fifty eyes of 50 patients (mean age 73.10; SD=5.36 years) with a diagnosis of mild AD and 152 eyes of 152 patients without AD (mean age 71.03; SD=4.62 years) were included. There was a thinning in the peripheral ring of the ganglion cell layer (GCL) in the AD group (S6  $p < 0.001$ ; T6 and N6  $p = 0.001$ ). In the superior sectors of the inner plexiform layer (IPL), differences between the two groups also remained statistically significant after Bonferroni correction (S3  $p = 0.001$  and S6  $p < 0.001$ ). Patients with AD showed a significant reduction in retinal layers and choroidal thickness. The thinnest macular measurements were found mostly in the inner layers, GCL and IPL, at superior pericentral and peripheral rings. This thinning may represent a possible retinal biomarker of AD, related with both primary retinal lesion and transsynaptic retrograde degeneration and the choroidal thinning probably reflects the importance of vascular factors in the pathogenesis of this disease.

2164

### Cholesterol and the extracellular deposits of age-related macular degeneration (AMD)

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**Summary:** AMD is a prevalent cause of central vision loss in older persons worldwide. The best documented intraocular risk factor for progression is drusen, i.e., extracellular deposits between the RPE basal lamina and the inner collagenous layer of Bruch's membrane. Clinicopathologic correlation, histochemistry for esterified and unesterified cholesterol (EC, UC), lipid-preserving ultrastructure, gene expression, and lipid profiling indicating enrichment in linoleate combine to suggest that the major component of soft drusen in central macula are large apolipoprotein B,E lipoproteins secreted by the RPE. This theory has received strong experimental support with a primary RPE cell culture system that lays down sub-RPE deposits without supplementation with outer segments. Through histologically-validated clinical imaging, a second layer of deposits between the photoreceptors and RPE, called subretinal drusenoid deposits is now recognized (SDD, originally called reticular pseudodrusen). Drusen have both EC and UC, and SDD have only UC. Further, soft drusen are abundant in central macula and SDD are abundant in the perifovea, thus linking distinctive cholesterol-containing deposits to the physiology of cone and rod photoreceptors.

2761

### Gene regulation and lens development: insights from single-cell RNA-seq analysis

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**Summary:** Lens progenitor cells emerge from a common pool of anterior pre-placodal cells located at the border between the neuroectoderm and surface ectoderm. Multiple lines of evidence exist to support critical roles of BMP and FGF signaling in this process. Our goal was to elucidate the complete transcriptome of lens progenitor and precursor cells. Human ES cells were differentiated into lens cells using noggin/BMP+FGF/FGF. In the second stage, BMPs were added  $\pm$  FGF2. The system was analyzed at between days 6–21 using single cell RNA-seq, using a PDMS co-flow microfluidic droplet generation device. Each cell was barcoded and sequenced using HiSeq2500 rapid mode. A total number of 25–30 000 of cells were captured and data were analyzed using tSNE. The proteomes of mouse lens were analyzed using tandem MS. DLX5 and FOXG1 expression are first activated followed by SIX1 and DLX2 expression. Evidence for common lens/olfactory is supported by the identification of ALDH1A3+/PAX6+/GATA3+ cells. Collectively, these studies show that lens cells are formed between days 12–18 of the cultures. Ongoing experiments are aimed to identify how BMP and FGF signaling direct formation of the lens progenitor cells.

T016

### Study of macular and optic disk blood flow by angio-OCT in Glucose-6-Phosphate Dehydrogenase (G6PD) deficient men and age-related G6PD-normal subjects

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**Purpose:** The reported prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency in Sardinia, Italy, ranges from 8% to 15%. Hemizygous males have totally deficient erythrocytes. Evidence indicates that patients with G6PD deficiency are protected against ischemic heart and cerebrovascular disease, colorectal cancer, retinal vein occlusion, and nonarteritic anterior ischemic optic neuropathy. The purpose of this study was to study the macular and optic disk blood flow by angio-OCT in G6PD-deficient men and age-related G6PD-normal subjects and ascertain whether, or not, there are statistically significant differences between the two groups

**Methods:** 22 G6PD-deficient men and 22 perfectly age-matched G6PD-normal controls were examined at the Ophthalmology Unit, University of Sassari, Sassari, Italy. A complete review of the medical history and a complete ophthalmological examination, including ETDRS best corrected visual acuity, slit-lamp biomicroscopy of the anterior segment, applanation tonometry, and fundus examination, was carried out. An HD 6-mm Angio-Retina and a 4.5-mm Angio Disk (RT-Vue, Optovue XR-100 with Angio Vue, CA) examination were also performed

**Results:** Only 1 eye per patients was included in the analysis, for a total of 22 eyes in each group. All the exported parameters about retinal and disk flow were evaluated. No statistical differences between the two groups were found, even after controlling for the effects of age, hypertension and hypercholesterolemia ( $p = 0.9$ ).

**Conclusions:** Results suggest that G6PD-deficient and G6PD-normal men have similar macular and optic disk blood flow. Larger scale studies are necessary to confirm these findings.

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**Comparison of collagen and alpha smooth muscle actin distribution in in-vitro and in-vivo developed posterior capsule opacification**

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**Purpose:** To compare the expression of collagen and alpha smooth muscle actin ( $\alpha$ SMA) in lens capsule samples after a short and long term post cataract surgery.

**Methods:** Twenty-four human donor eyes were obtained, and separated in to three different groups: IOL capsules ( $n = 12$ ): lens capsules with IOLs and varying degrees of Soemmering's ring formation, Cultured capsules ( $n = 6$ ): emptied capsular bags, cultured for 1-month and Intact lenses ( $n = 6$ ). All samples were stained with H&E,  $\alpha$ SMA and Picro Sirius Red for collagen I, III and IV.

**Results:** All Cultured capsules except one, expressed  $\alpha$ SMA which tended to concentrate near the capsule. IOL capsules only expressed  $\alpha$ SMA in areas where the capsules adhered to each other. Intact lenses did not express  $\alpha$ SMA. All samples expressed collagen I and IV in the lens capsules, and collagen I and III in the ciliary muscles. None of the Intact lenses or Cultured capsules expressed collagen in any other areas. Seven of the twelve IOL capsules expressed collagen I and III in their Soemmering's rings where the anterior rhexis and posterior capsules contacted the IOL. These areas were also the only ones that expressed  $\alpha$ SMA.

**Conclusions:** In the short term after cataract removal (Cultured capsules),  $\alpha$ SMA was found throughout all cells, adhering the capsules together. In the long term (IOL capsules), both  $\alpha$ SMA and collagen were found near the IOL, creating a type of seal.

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**The 100 000 genomes project and the Western Eye Hospital experience**

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**Purpose:** Genetic eye diseases are extremely heterogeneous both in terms of possible phenotypes and related molecular causative defects.

Any part of the visual system can be affected with an extremely high number of conditions that recognize a genetic defect as the primary cause. To date at least 600 genes are considered as involved in both isolated and syndromic forms of genetic eye diseases, but yet the genetic cause remains unidentified in a significative percentage of patients.

Despite the high number of identified genes causing ophthalmologic diseases and the new available advanced sequencing facilities, a consistent percentage of patients will not have access to molecular genetic diagnosis.

**Methods:** At the Western Eye Hospital an integrated diagnostic pathway has been created in collaboration with the 100 000 Genomes Project, a UK Government project, aiming at the identification of genetic defects related to cancer and rare diseases (including

ophthalmological) through whole genome sequencing in National Health Service (NHS) patients.

**Results:** Patients are given the opportunity to receive a one-stop care including clinical and instrumental investigations (including imaging and electrophysiology), counselling and genetic testing. Results from genetic testing are related to phenotype and discussed in a multidisciplinary context. Segregation studies are then carried out both to validate results and as a diagnostic tool to family members.

**Conclusions:** The identification of causative genes and eventually novel genes and pathogenic mechanisms leads to multiple benefits, from the precise definition of clinical entities, to the possibility to provide focused genetic counselling to patients and their family members. Finally, this is a crucial step towards patients' recruitment in possible experimental therapeutic strategies.

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**Mycotic keratitis – the threat of today?**

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**Summary:** Mycotic keratitis is a comparatively rare but serious ophthalmological disease, that can possibly lead to a severe loss of vision up to blindness. Over the last two decades an increase of cases with mycotic keratitis has been noticed, which is possibly caused by an increased use of soft contact lenses. In this talk we would like to give an overview on the typical clinical signs, symptoms, diagnostics and therapy as well as new diagnostic methods of keratomycosis.

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**Intracorneal ring segments (INTACS) – long-term results of the first 100 keratoconus patients**

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**Summary:** Implantation of intracorneal ring segments (ICRS) using a femtosecond laser represents a reliable option to widen the spectrum of the stage-related therapy of keratoconus in patients with contact lens intolerance, post-LASIK-keratectasia, or pellucid marginal degeneration (PMD).

Between August 2011 and February 2018, ICRS (Intacs-sk, Addition Technology, Inc.) were implanted in 101 eyes of 81 patients with clear central cornea. The patients had to fulfill the corneal diagnostic criteria required for implantation. Tunnel creation should nowadays only be carried out by femtosecond laser, in order to avoid intra- and postoperative complications.

Two years after surgery, the patients showed an increase in uncorrected (logMAR) from  $0.9 \pm 0.1$  to  $0.4 \pm 0.1$  and bestcorrected distance visual acuity (logMAR) from  $0.4 \pm 0.2$  to  $0.2 \pm 0.1$ .

Uncorrected and corrected distance visual acuity can be improved by implantation of the ICRS. Progression of ectasia seems to be retarded. Complications after ICRS implantation are rare due to strict patient selection and modern surgical techniques.