**OP-1**

CONJUNCTIVAL GENETIC ‘FINGERPRINTING’ IN OCULAR MUCOUS MEMBRANE PEMPHIGOID

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Objective Ocular Mucous Membrane Pemphigoid (OcMMP) is a rare disease characterised by chronic autoimmune-driven conjunctival inflammation leading to progressive scarring, and blinding sequelae. The purpose of this study was to characterise the conjunctival gene ‘fingerprint’ involved in the fibrosis signalling pathways in the pathogenesis of OcMMP.

Methods and Analysis Ocular surface gene expression studies were undertaken on conjunctival swabs from OcMMP and age-matched control patients. The NanoString nCounter Human Fibrosis panel (NanoString Technologies Inc.) quantified RNA expression from 770 genes. Differentially expressed genes (DEG) and pathway analysis were determined using HyperScale architecture designed by ROSALIND, Inc. with normalisation, fold changes (≥1.5-fold or ≤-1.5-fold) and p-values adjustment (<0.05) using the Benjamini-Hochberg method. Significantly identified genes were aligned to the aldehyde dehydrogenase (ALDH) retnoic acid fibroblast autoregulation conjunctival scarring signalling pathway, known to be central to immune-mediated mucosal scarring in OcMMP.

Results 6 OcMMP patients (8 eyes, mean age 76.5 (±7.0 SD) years, 6 (66%) male, 3 (50%) biopsy-positive) and 8 age-matched cataract patients (15 eyes; age 73.1 (±9.3) years, 3 (37%) male), serving as controls were analysed. Ninety-three DEGs were observed between OcMMP and controls (48 upregulated and 45 downregulated). Of these, the top 10 upregulated DEGs were COL3A1, COL1A1, FN1, TPSAB1/B2, THBS1, SERPINE1, SPP1, COL5A1, OASL and IL1B. 44 pathways that had a global significance score greater or equal to 2, the most significant representing extracellular matrix (ECM) remodelling, synthesis, and degradation.

Conclusion The conjunctival genetic ‘fingerprint’ predominantly suggests an activated fibroblastic phenotype in the OcMMP patients and could represent (i) novel targets for drug discovery and (ii) surrogate outcomes/novel biomarkers for the monitoring of disease progression.

**OP-2**

LONG-TERM OUTCOMES OF REBUBBLING AND GRAFT DETACHMENT IN DESCemet MEMBRANE ENDOTHELIAL KERATOPLASTY USING A STANDARDISED PROTOCOL

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Objective To analyse risk factors and long-term outcomes after rebubbling and graft detachment in Descemet membrane endothelial keratoplasty (DMEK).

Methods and Analysis 176 consecutive DMEK grafts of 125 patients performed by 8 surgeons with a standardised technique between January 2015 and January 2022 were analysed. Main outcome measures were graft detachments, rebubbling rate, postoperative outcomes, and risk factors for graft failure and rebubbling.

Results 6 (3.4%) grafts required rebubbling (<1/3 detached). 41 (23%) grafts developed self-resolving partial detachments (<1/3 detached). 5-year graft survival were 96%, 87%, and 83% in fully attached, partially detached and rebubbled eyes. Percentage endothelial cell loss (ECL) was 57.5±14.1, 57.9±14.2, and 68.8±8.8 (p=0.035) in fully attached, partially detached and rebubbled eyes. Graft failure occurred in 9 (5.1%) eyes: 3 grafts had primary failure, 2 had early failure (<3 months), 2 had late failure (<12 months), and 2 grafts did not fully unfold intraoperatively. Intraoperative trauma (score) was a risk factor for graft failure (HR 1.81; 95% CI: 1.33–2.50 (p=0.0229)). Indication for surgery was a risk factor for rebubbling (HR 5.28; 95% CI: 5.11–72.4 (p=0.00703)).

Conclusion DMEK grafts had better graft survival if there was no partial detachment or rebubbling up to 5 years postop. There was significant ECL associated with rebubbling. A standardised technique reduces rebubbling and graft failure risk.

**OP-3**

PERSONALISED MODEL TO PREDICT KERATOCONUS PROGRESSION FROM DEMOGRAPHIC, TOPOGRAPHIC AND GENETIC DATA

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Objective To generate a personalised prognostic model to predict keratoconus progression to corneal collagen cross-linking (CXL).

Methods and Analysis In this retrospective cohort study, we recruited 5,025 patients (9,341 eyes) with early keratoconus between January 2011 and November 2020. Genetic data from 926 patients was available. We evaluated both change in keratometry or CXL as indices of progression and used the Royston-Parmar method on the proportional hazards scale to generate a prognostic model. We calculated hazard ratios (HR) for each significant covariate, with explained variation and discrimination.

Results After exclusions, model-fitting comprised 8,701 eyes, of which 3,232 underwent CXL. For early keratoconus CXL provided a more robust prognostic model than keratometric progression. The final model explains 33% of the variation in time-to-event age HR [95% confidence limits] 0.9 [0.90–0.91], maximum anterior keratometry (Kmax) 1.08 [1.07–1.09], and minimum corneal thickness 0.95 [0.93–0.96] as significant covariates. Single nucleotide polymorphisms (SNPs)