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Can Aqueous Proteomics Predict the Recurrence of Rhegmatogenous Retinal Detachment?

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Summary Statement: Aqueous proteome collected at primary surgery in patients who eventually suffer recurrent retinal detachment due to PVR, differs from patients who do not. Enriched and or exclusive proteins include cell-cell and cell-matrix adhesion and mechano-transduction molecules.

Abstract

Purpose: To explore whether the proteome of aqueous collected during primary repair of rhegmatogenous Retinal Detachment (RD), differs between patients who experience recurrency (Recurrent RD Group) and those who do not (No Recurrent RD Group).

Methods: The aqueous proteome collected during primary surgery of 13 patients undergoing Recurrent RD was compared to 11 age and sex-matched patients successfully operated for rhegmatogenous RD with no recurrency after 12-months follow-up, regardless of surgical technique. A label-free shotgun proteomics approach identified and quantified the repertoire of aqueous proteins. Differential protein expression between Groups was determined using the Limma moderated Bayesian t-test, followed by False Discovery Rate (FDR) validation using Storey's q-test.

Results: Aqueous profiling identified >800 unique proteins; 45 exclusive to the Recurrent RD group, 10 exclusive to the no Recurrent RD group and 33 differently expressed between groups (log2fold-change≥ | 0.57 |, FDR≤0.05). Proteins upregulated in Recurrent RD patients, clearly pointed to mechanisms of cell:cell and cell:matrix adhesiveness and mechano-transduction signalling pathways. Upregulated proteins included extracellular matrix components such as type I and IV collagens, bi-glycan, proteoglycans, and cell-membrane adhesion molecules.

Conclusion: The baseline aqueous composition of RD patients that will eventually develop recurrency, differs significantly from those who will not, and already contains molecular signatures that may help identify the risk of recurrency at the time of primary repair. While acknowledging the pilot nature of the study, our findings strongly suggest that Recurrent RD is associated with cell adhesiveness pathways early alterations, offering targets for prognostic assessment and therapy.

Introduction

Rhegmatogenous Retinal Detachment (RD) is a severe ocular condition whose incidence is reported between 10-17/100,000 cases per year with an increasing trend in the past decades[1–4].

Recurrent Retinal Detachment (Recurrent RD) develops in 18-22% of patients undergoing primary repair[5–7] and retains a guarded prognosis in a relevant proportion of affected patients, potentially leading to blindness[8]. Proliferative Vitreoretinopathy (PVR) is the primary cause of recurrent RD and originates from a cascade of events including RPE cells migration in the vitreous chamber[9], phenotypic conversion to matrix-producing fibroblasts and myofibroblasts (the epithelial-mesenchymal transition; ETM)[10], extra-cellular matrix deposition[9] and membrane contraction leading to recurrent RD[11].

The reason why some RD patients develop PVR and experience recurrent RD remains unclear; genetic[12,13], social[14] and acquired factors[15] have all been investigated, but to date there is no established biomarker retaining prognostic value and no validated therapy.

High resolution proteomics is a relatively young discipline, intended to study the entire array of synthesized proteins (the *proteome*), their post-translational modification and/or degradation in tissues or biologic fluids and had been applied to retinal detachment before[16].

The purpose of present paper is to compare the array of proteins expressed at the time of primary surgery in the aqueous of patients who will then recur, with those present in the aqueous of patients who will not, in order to identify if there were protein signatures already differently activated before surgical repair and capable of determining the subsequent evolution.

Materials and Methods

Study Participants

The medical records of all patients undergoing surgery for primary RD at the IRCCS Fondazione Bietti ONLUS between October 2023 and April 2024 and aqueous collection, with at least 12 months follow-up were revised. As of November 2025 (month of submission of this manuscript), No Recurrent RD subjects were still free of RD recurrence. After the exclusion of patients with incomplete charts or no viable aqueous sample, 13 patients developing PVR and recurrent RD after initially successful primary RD repair were identified and matched for age and sex with 11 patients operated during the same time frame and free of recurrence at the 12-month follow-up visit.

The study followed the Tenets of the Helsinki Declaration and received institutional approval (ERMLAB01 N° 77/18/FB)

Specimen Collection

At the very beginning of surgery, after sterile draping and povidone iodine rinsing, 1ml of aqueous of was withdrawn from the anterior chamber with a 30G needle and immediately stored at -80°C.

Proteome Analysis

Sample Processing and Preparation

Samples were cleared by centrifugation and stored at −80 °C until use. The protein concentration of each sample was determined using the Bicinchoninic Acid (BCA) assay

(Fisher Scientific, Waltham, MA, USA). For subsequent shotgun proteomics analysis, 10 µg of protein from each sample was addressed to trypsin digestion.

Protein Digestion and Cleanup

The fluid was first dried using a Speed-Vac concentrator and then resuspended in a 2 M guanidine-HCl solution, as described elsewhere (Zingale et al., 2025, Sci Report). Samples were digested with mass-grade trypsin (enzyme:protein ratio of 1:40) (Fisher Scientific, Waltham, MA, USA) overnight at 37 °C. Digestion was quenched by adding 0.4 percent trifluoroacetic acid (TFA). The resulting peptides were then cleaned and desalted using C18 StageTips (Fisher Scientific, Waltham, MA, USA).

Mass Spectrometry Analysis

One µg of purified tryptic peptides was injected into an Orbitrap Exploris 240 mass analyzer online with a nanoHigh Performace Liquid Chromatography (nHPLC) system. The instrument was configured in Data-Dependent Acquisition (DDA) modality for label-free quantification.

Proteomic Data Processing and Protein Identification

Proteomic analysis was run on a single-subject scale using the Inferys rescoring algorithm implemented in Proteome Discoverer (PD) v2.5 software. Raw spectra were searched against a human FASTA database (including canonical and non-canonical proteins) using the Sequest HT and Inferys rescoring algorithms. A list of common contaminant proteins was included in the search criteria. Peptide Spectrum Matches (PSMs), which link an observed tandem mass spectrum to a peptide sequence, were

filtered at a False Discovery Rate (FDR) ≤0.05 using a concatenated target-decoy search strategy implemented in Percolator.

Data Analysis and Statistics

Demographics statistics used t-test for numerical variables and chi-squared test for nominal ones, significance was set at the 0.05 level in all cases.

Unless otherwise indicated, all data analysis used in-house built R-Studio (v4.5.1) scripts, which incorporated standard and specialized R libraries to facilitate data cleaning, transformation, statistical analysis, and visualization.[n]. A class-specific quantile normalization was used to normalize protein intensities. Thereafter, a Classification and Regression Tree (CART) method was used to impute the missing values[17].Differentially Expressed Proteins (DEPs) were then identified using a moderated Bayesian t-test implemented in Linear Models for Microarray Data (Limma) implemented in "*limma*" R package[18] Proteins were defined as DEPs with log2FC≥｜0.57｜ and p≤0.05 after Storey's q value for FDR control (q.mod) using the "*qvalue*" package in R.

To cluster and rationalize data, DEPs, along with those identified as exclusive to either the recurrent RD or No Recurrent RD groups, were then submitted to protein-protein interaction (PPI) analysis using STRING Network software (v12.1) using the k-means clustering option. Moreover, Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) were used to analyze the data. Identified terms were first filtered for p-value adjusted by Benjamini-Hochberg correction (FDR) ≤0.1[19].

Results

The demographics, systemic, and clinical findings on presentation are reported in Table 1 for both groups. There were not statistically significant differences: mean age was

63.3±4.2 years in the No Recurrent RD Groups and 62.7±9.7 in the Recurrent RD Group (p=0.853); the male/females ratio was 5/6 in the No Recurrent RD group and 9/4 in the Recurrent RD Group (p=0.239) as age and sex were matched by study design, neither were significant the PVR grade[1] (p=0.360), type of primary surgery (p=0.729), pseudophakic status (p=0.193) and associated systemic illnesses.

The study identified and quantified 828 proteins (FDR≤0.05) with a robust overlap between Recurrent RD and no-Recurrent RD groups: 773 proteins were consistently identified in both groups, 10 individual proteins were identified exclusively in the No Recurrent RD group, and 45 exclusively in the Recurrent RD group (Figure 1; see Appendix for additional quality metrics).

Quality control metrics ruled out technical issues. A box-plot of non-normalized log-2 protein intensities showed similar median values and distribution across all samples pre- and post-quantile normalization (Supplemental Figure 1). Furthermore, a density plot of log2-transformed intensities (pre- and post-normalization) showed a comparable, bell-shaped distribution across all samples (Supplemental Figure 2).

The Principal Component Analysis (PCA) exploring the global features of the two groups showed a significant overall distinction between Recurrent RD and No Recurrent RD patients, as the pink and blue dots (and the respective elliptic areas) shown in Fig. 2 do not overlap at all and cluster in distinct areas of the plot.

Of the 773 unique proteins identified in both groups, 23 were found significantly upregulated and 11 proteins were found downregulated in the Recurrent RD/No Recurrent RD ratio (Fig. 3 and Supplemental Tables 1).

Submission of the downregulated (Recurrent RD/No Recurrent RD ratio) and No Recurrent RD exclusive proteins to PPI analysis did not retrieve any evidence of enriched terms or pathways. Conversely, the repertoire of upregulated (Recurrent RD/No Recurrent

RD ratio) and Recurrent RD-exclusive proteins revealed a highly significant functional signature pertaining to the pathology (PPI enrichment p-value = 0.00269). These proteins were found to group into nine distinct clusters depicted in different colors in Fig.4 (Supplemental Table 2).

Focusing on clusters with more than 3 member proteins, a prominent feature was the enrichment of proteins with key and proven roles in extracellular matrix (ECM) composition and remodeling, including biglycan and type I/type IV Collagen. Furthermore, we identified proteins involved in cell-cell adhesion and cell-matrix adhesiveness, such as desmocollin, plakoglobin (a key component of desmosomes), filaggrin-2, talin-1 (a critical link between integrins and the actin cytoskeleton), and cadherin-6.

In addition to these ECM and adhesion-related proteins, the analysis robustly identified upregulated proteins central to signaling pathways that regulate cell adhesiveness and cytoskeletal dynamics and, remarkably, signaling pathways regulated through G-proteins. These include Rho-Dissociation Inhibitor-1 and -2 (RhoGDI1/2), transforming protein RhoA (a major component of the Rho GTPase signaling axis), and elongation Factor-1 and -2 (EF-1/2). Within the same biological clusters, we also identified soluble mediators of immunological and inflammatory processes, notably Processed Macrophage Colony-Stimulating Factor 1 (M-CSF1).

To further rationalize the biological data, the repertoire of upregulated (Recurrent RD/No Recurrent RD ratio) and Recurrent RD exclusive proteins were submitted to KEGG analysis. This approach retrieved the enrichment of different terms encompassing focal adhesion and rap1 signaling pathways, which identifies a G-proteins regulated cascade involved in cell adhesion and cell:cell junction formation and platelet activation (FDR≤0.05). By relaxing the FDR (≤0.075), cytoskeleton in muscle cells and motor proteins were further identified. A confirmatory GO analysis identified enrichment of

biological process (BP) terms consistent with KEGG outcome, but with FDR≤0.075 (fig. 5).

In particular, among enriched terms in the BP chart (Fig. 5A), our analysis identified tissue morphogenesis, cell:cell junction assembly and organization, and several terms associated with G-proteins signaling pathways. Finally, in accordance with this finding, a Principal Coordinate Analysis (PCoA, Fig. 5C), and the related three map plot (Fig. 5D), pointed out the enrichment of four main clusters, namely: cell:cell junction assembly, regulation of cell:matrix adhesion, adenylate-cyclase modulating G protein-coupled receptor signaling pathway, and morphogenesis of a branching structure.

Discussion

Recurrent retinal detachment due to PVR after primary successful repair represents the most dreaded *sequelae* of retinal detachment surgery, claiming a heavy tribute in terms of vision and patients' quality of life. Previous studies on the proteomics of RD and PVR unveiled alterations of the complement, coagulation, extra-cellular matrix remodelling as well as glycolysis and oxidative stress metabolisms, however failing to identify overt and consistent biomarkers and/or newer therapeutic approaches[5,16,20–30].

The shot-gun proteomics analysis we run, reveals that the baseline aqueous proteome of patients who eventually recurred, differs significantly from that of the no-Recurrent RD Group, despite age and sex matching and, more importantly, no significant difference on baseline PVR grading between groups.

Interestingly, since aqueous was collected at the very beginning of the primary repair surgery, irrespective of chosen technique (scleral buckling or *pars plana* vitrectomy), the identified proteomic differences represent molecular conditions present at the time of primary detachment and already potentially responsible for the eye's fate.

The robustness of proteomic differences between groups is supported by non-normalized and normalized protein intensity distribution plots (see appendix, supplemental fig. 1 and 2), showing consistent results and minimal intra-group variability. Although the net separation across PC1 and PC2 was relatively small (fig. 2), all patients belonging to different groups were consistently distinct, suggesting small but constant differences between the two proteomes (Supplemental Fig. 1 and 2).

The biological and translational potential of these findings is indirectly strengthened by the concentration of key differences within specific, functionally relevant clusters clinically related to Recurrent RD pathogenesis. Specifically, KEGG and GO analyses identified cell adhesiveness, extracellular matrix (ECM) composition, and signalling pathways generally associated with cellular mechano-transduction as the primary clusters enriched in the Recurrent RD group compared to the No Recurrent RD group (fig. 4 and 5).

Within these enriched terms, we observed the upregulation of critical ECM components, including type I collagen, the main component of fibrillar collagen and ECM ultrastructure, and type IV collagen, a major component of reticular collagen and basement membranes[31,32]. Furthermore, the increased presence of the associated molecule biglycan, which is fundamental for ECM ultrastructural homeostasis and remodelling as well as for inflammation, draws specific attention to dysregulated processes of cell adhesiveness to the surrounding matrix[33,34]. In addition to these structural ECM proteins, the analysis identified membrane proteins, such as cadherin-6 and talin-1, which serve pivotal roles in cell:cell and cell:matrix interactions, respectively in addition to other cell adhesion-related molecules such as plakoglobin and desmocollin[35].

Along with the extracellular or membrane-bound proteins, we also found several Rho factors and proteins involved in G-receptor signalling such as Rho-dissociation GDP inhibitor -1 and -2, calmodulin-1, transforming protein Rho-A[36].

More specifically, Rho proteins are small GTPases that act as molecular switches downstream of various receptors, including G-protein coupled receptors (GCPRs), which are often involved in cell signalling[36,37]. Rho-A is a central player in regulating the actin cytoskeleton, controlling cell shape, motility, and contractility, and it is activated by mechanical stress (structural *stimuli*) and biochemical cues (receptor signalling). In general, the Rho/ROCK pathway influences the formation of focal adhesions (cell-to-matrix contacts) and *adherens* junctions (cell-to-cell contacts), which anchor the cell to the ECM and transduce mechanical tension across the cell.

Therefore, this evidence suggests that a concerted and multi-faceted repertoire of proteins responsible for transducing mechanical and structural stimuli to the cell is dysregulated in patients destined to recurrent RD, well before such a re-detachment occurs and even before the (initially successful) primary repair.

Bearing in mind that the aqueous is an extracellular environment, the presence of components related to membrane-bound or even intracellular proteins, further suggests dynamic intracellular compartmentalization and trafficking, while collagen proteins point directly to active ECM turnover. In a similar context, Yu and colleagues[25] found an overexpression of proteins related to inflammation, cell adhesion, and specifically the complement and coagulation cascades when comparing PVR vitreous samples to normal corneal donors[25].

We acknowledge that proteins identified through a shotgun proteomics approach are, in most cases, those more amenable to trypsin processing *in vitro*. Therefore, the reported findings may also reflect unexplored processes and pathways primarily driving the

increased risk of developing recurrent RD, such as aberrant proteolytic processing of ECM and cellular proteins *in vivo*. Such changes could anticipate the release of both structural and non-structural components, thereby promoting their susceptibility to digestion.

In this regard, a recent study by our group explored the degradome of the vitreous[38], which, given its higher protein and volume availability, is more amenable to complex analyses than the aqueous. That work identified a repertoire of endogenous proteolytic events by comparing RD patients to those undergoing surgery for non-RD conditions (e.g.: idiopathic epiretinal membranes). While that study uncovered an altered pattern of proteolysis of the vitreous body's structural and non-structural components, none of the specific proteins identified in the aqueous of present study were documented to undergo aberrant proteolysis in the vitreous, at least under the analytical settings used (which did not distinguish between No Recurrent RD and Recurrent RD).

In conclusion, although the pathogenesis of Recurrent RD remains largely unknown, especially in the setting of non-syndromic primary RD representing most cases and in which genetics seem to play a lesser role[14], our study clearly identifies different proteome signatures between groups, offering several promising targets for future investigation. To date, in fact while the cascade of events leading to PVR and Recurrent RD in a steady proportion of cases across published series, is relatively well-known, but what triggers it and why, remains elusive[2].

This pilot study provides solid proteomics evidence that the aqueous of Recurrent RD and No Recurrent RD patients macroscopically and significantly differ for the relative presence of dozens of proteins that strongly point to a specific pre-existing configuration. All those cellular domains appeared active in the aqueous of RD patients at the time of primary detachment repair as if the destiny of those eyes undergoing a recurrency were already determined.

From the clinically perspective, and if further confirmed, this scenario would allow the active search for biomarkers of Recurrent RD, to be found within the array of proteins differently expressed across the two groups. It should also be noted that the aqueous proteome alterations we identified, most likely represent the reflection of pathological processes developing in the vitreous chamber where PVR ensues and possibly offers the proof of concept that aqueous specimens may be a useful proxy of vitreous at least in this case. Given the relative ease of aqueous specimen collection and harvesting through minimally invasive procedures, compared to vitreous tap, this may open the way to further diagnostics.

In summary our data suggest the unprecedented possibility of identifying at the time of primary repair the eyes destined, or more prudently at higher risk for Recurrent RD, which, potentially, would allow a selective targeted treatment to minimize such occurrence.

Data Availability Statement: The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium (http://proteomecentral.proteomexchange.org) via the PRIDE partner repository. **Project accession:** PXD070155; **Token:** DE2SkSfu 54jk. Alternatively, data can be seen by logging in the PRIDE website using the following account details: **Username**: reviewer_pxd070155@ebi.ac.uk; **Password**: 8XQcoL8OgHVm.

This manuscript has no supplemental digital contents

Appendix

Supplementary Figure 1

Supplementary Figure 2

Supplementary Table 1

Supplementary Table 2

Figure Caption

Fig. 1 – Venn's diagram showing proteome overlapping: The central overlapping area (*pink*) shows the 773 proteins common to both groups. The left crescent (*blue*) represents the 10 proteins exclusive to the No Recurrent RD Group, and the right crescent (*red*) represents the 45 proteins exclusive to the Recurrent RD Group.

Fig. 2 - Principal Component Analysis (PCA) of aqueous proteomes. The plot shows the separation between the Recurrent RD Group (pink dots/area) and the No Recurrent RD Group, (blue dots/area) groups based on their protein expression profiles. PC1 and PC2 capture X% and Y% of the total variance, respectively.

Figure 3 – Volcano plot showing the outcome of Limma analysis on 771 proteins identified and quantified in both groups. The dashed horizontal line marks the -log10 value of the FDR (q value) computed by Storey's test. This threshold was set to 1.3, which corresponds to FDR≤0.05. The 2 vertical dashed lines mark the log2 threshold, set to |0.57| for protein intensities in the Recurrent RD/No Recurrent RD ratios. Blue dots in the upper left quadrant represent proteins significantly downregulated in the Recurrent RD Group compared to the No Recurrent RD Group and the red dots in the upper right quadrant represent the proteins significantly over-expressed in the RD Group compared to the No Recurrent RD group.

Figure 4 – PPI network identified by submitting proteins upregulated in the Recurrent RD/no Recurrent RD ratio and exclusive of Recurrent RD subjects to STRING Network analysis. The analysis was done using the k-means clustering option. Proteins are identified by their gene name. Different colors identified the n=9 individual clusters identified through the analysis. The higher the density of lines bridging the proteins, the higher the confidence of PPI within each individual cluster. The color-code matches those indicated in Supplemental Table 2, which shows the cluster composition and features including Gene names shown in figure.

Figure 5 – (A) KEGG chart generated by submitting proteins upregulated in the Recurrent RD/no Recurrent RD ratio or exclusive of Recurrent RD to KEGG analysis. Enriched terms were filtered for p-value adjusted (p.adjust) by BH correction ≤0.1. Cell adhesion, Rap1 signaling pathway and platelet activation showed FDR≤0.05. Gene count is further shown by dot size; (B) Biological Processes enrichment chart generated submitting the same list of proteins analysis in (A) to Gene Ontology. In this case, terms shown in the plot were identified with FDR ≤0.075; (C) PcOA analysis showing the main 4 clusters identified through the terms enriched in Recurrent RD aqueous proteome; (D) TreeMap plot of the terms associated to the 4 clusters identified by the PcOA analysis. Note that the tree maps group enriched GO terms into functional clusters (colored blocks) and size them by enrichment strength (e.g. −log10 p value or term size).

Supplementary Figure 1--http://links.lww.com/IAE/C823

Supplementary Figure 2--http://links.lww.com/IAE/C824

Supplementary Table 1--http://links.lww.com/IAE/C825

Supplementary Table 2--http://links.lww.com/IAE/C826

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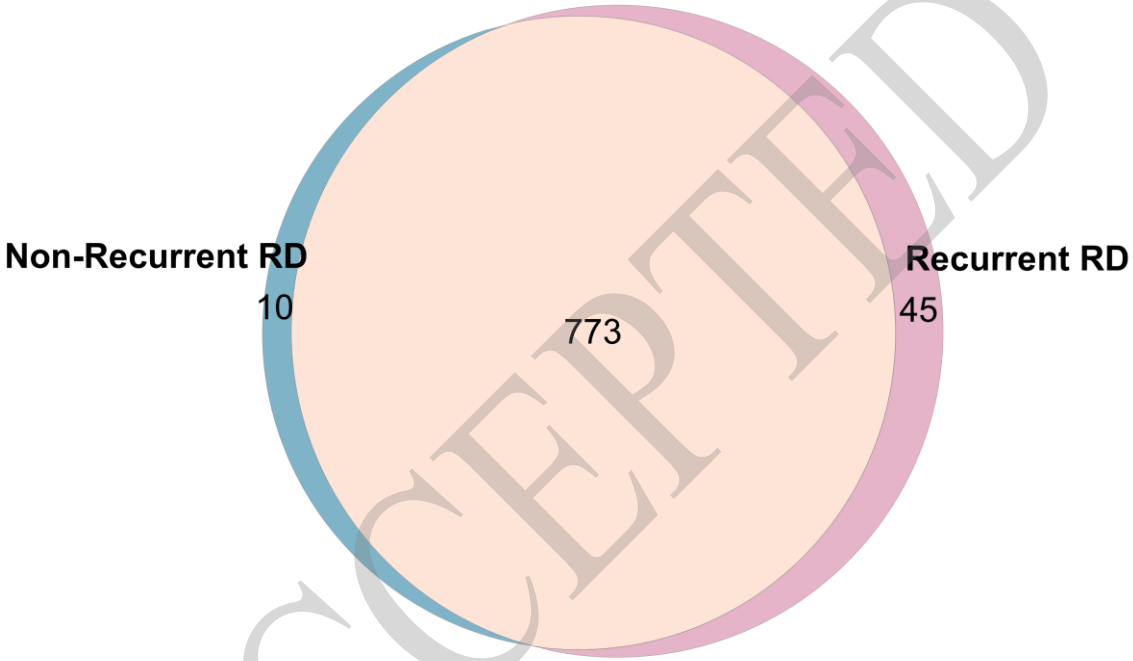

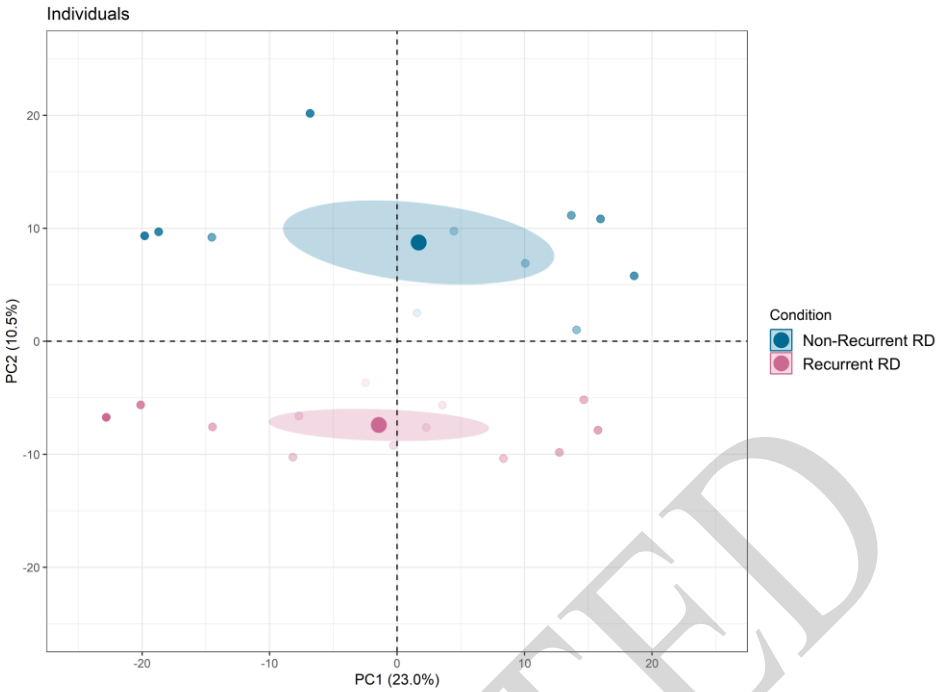

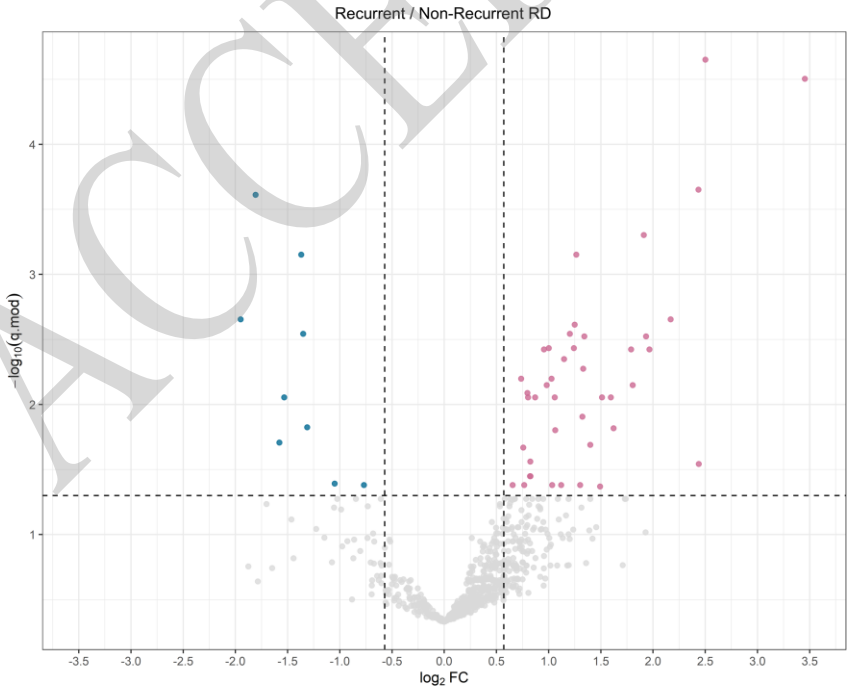

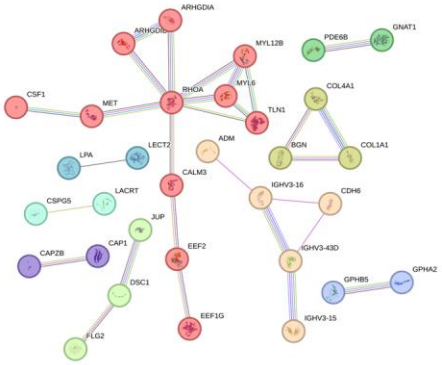

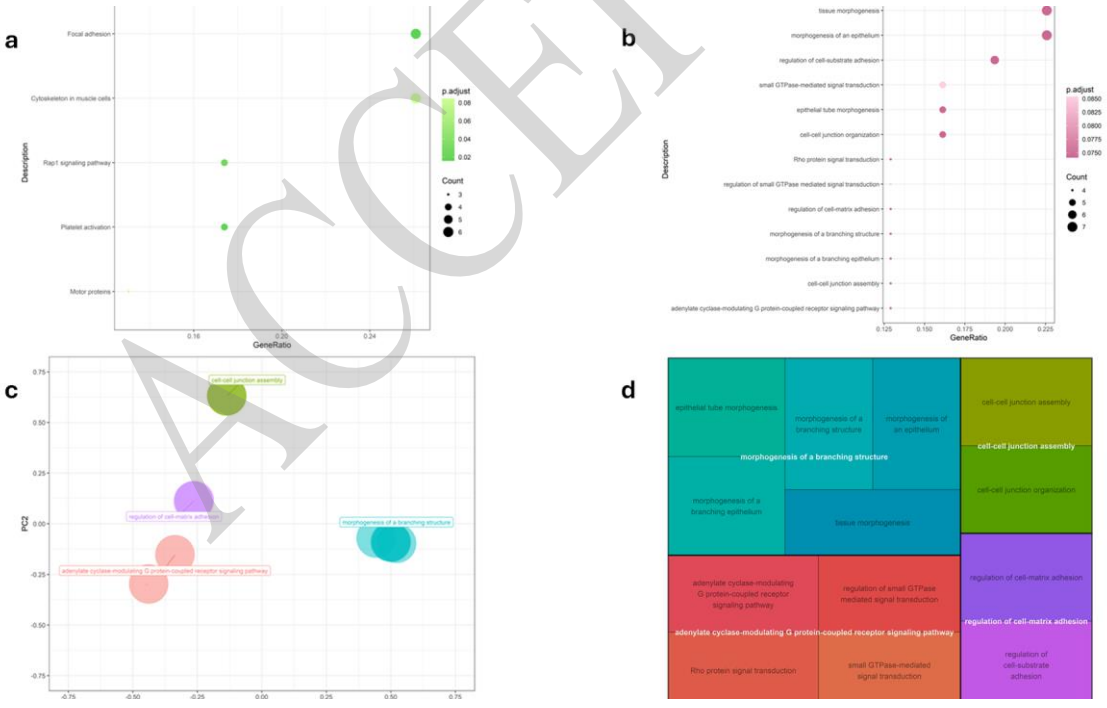

Non-Recurrent RD Group											
ID	**M/F**	**Age**	**Eye**	**BCVA**	**N and Localization of RB**	**Duration of symptoms**	**PP**	**PVR Grade**	**Surgery**	**Clinical History**	**Eye Diseases**
1	M	62	L	20/400	1 h 3	3 days	No	b	SB	-	-
2	F	67	L	HM	1 h 12	9 days	No	b	SB	SH	-
3	M	63	L	20/1000	1 h 1	4 days	No	b	PPV C3F8	Prostatic hypertrophy	-
4	M	63	R	HM	1 h 4	4 days	No	c	PPV C3F8	Rheumatic polymyalgia	Glaucoma
5	F	67	L	HM	1 h 1	3 days	No	b	SB	NIDDM, SH, hypercholesterolemia	-
6	M	62	R	HM	3 h 7-8-9	4 days	Yes	c	PPV SiO	-	-
7	F	62	L	HM	1 h 12	8 days	No	b	SB	SH	-
8	F	61	L	LP	1 h 1	2 days	No	b	SB	SH, hypercholesterolemia	-
9	M	54	R	HM	3 h 9-11-12	4 days	No	c	SB	-	-
10	F	66	L	20/400	1 h 5	1 day	No	c	PPV C3F8	-	-
11	F	70	R	20/400	1 h 7	5 days	No	b	PPV C3F8	SH, hypercholesterolemia	-
Recurrent RD Group											
ID	**M/F**	**Age**	**Eye**	**BCVA**	**N and Localization of RB**	**Duration of symptoms**	**PP**	**PVR Grade**	**Surgery**	**Clinical History**	**Eye Diseases**
1	M	71	L	20/400	1 h 8	12 days	Yes	b	PPV C3F8	-	OHT
2	F	54	R	20/400	1 h 10	3 days	No	b	SB	-	-
3	M	58	R	HM	1 h 10	3 days	No	a	SB	Prostatic hypertrophy	-
4	M	67	L	CF	1 h 11	1 day	No	b	SB	SH, AMI, hypercholesterolemia	-
5	F	56	R	HM	2 h 1-2	2 days	No	b	SB	SH	-
6	M	69	L	HM	1 h 2	1 days	No	b	SB	SH, hypercholesterolemia	-
7	M	64	L	HM	1 h 7	2 days	Yes	c	PPV C3F8	-	OHT
8	F	59	R	20/25	1 h 12	6 days	No	b	SB	-	-
9	M	49	R	20/32	1 h 1	4 days	No	b	PPV SF6	-	-
10	M	83	L	HM	2 h 3-4	3 days	Yes	b	PPV C3F8	SH, hypercholesterolemia	OHT
11	F	67	L	20/400	1 h 11	8 days	Yes	c	PPV C3F8	Hypothyroidism	-
12	M	49	L	HM	1 h 1	3 days	No	c	SB	Asthma	-
13	M	70	L	HM	1 h 3	2 days	No	b	SB	SH, hypercholesterolemia	-

Table 1 – Demographics, ocular and systemic findings - RD: Retinal Detachment; BCVA: Best Corrected Visual Acuity (Snellen); RB: Retinal Break; PP: Pseudophakia; PVR: Proliferative Vitreoretinopathy; HM: Hand Motion; CF: Counting Fingers; SB: Scleral Buckling; LP: Light Perception; SiO; Silicone Oil; OHT: Ocular Hypertension; AMI: Acute Myocardial Infarction; SH: Systemic Hypertension; NIDDM: Non Insulino-Dependent Diabetes Mellitus.