

**Supplementary files** 

Supplementary figure 1 Quality control of single-cell transcriptome profiles of 5 independent FVM samples

- (A) Log10-transformed genes per UMI for each cell in comparison among the three samples.
- (B) Correlation of genes (nFeature\_RNA) with UMI (nCount\_RNA) in each cell among the three samples.
- (C) UMAP plot of single cells from each sample.



## Supplementary figure 2. Selected gene expression in all detected cells on FVM

(A) UMAP plot showing the specific expression of *COL1A1*, *CD2*, *VWF* and *CD1C* in mesenchymal cell, T lymphocyte, endothelium and dendrite cell, respectively.

(B) UMAP plot showing the expression of microglia-enriched marker C1QA and GPR34 on FVM.

(C) UMAP plot showing the expression of representative marker genes of each subtype of microglia on FVM.

(D) GSEA analysis showing that genes upregulated in GPNMB<sup>+</sup> microglial subtype were enriched for genes associated with lipid metabolism and fibrillar structure.

(E) GSEA analysis showing that genes upregulated in MRC1<sup>+</sup> microglial subtype were enriched for genes associated with humoral immune response and complement activation.



Supplementary figure 3 The extraction of homeostatic retinal microglia from published single-cell data of adult human retina (A-B) The distribution of each microglial subtype marker in C1QA<sup>+</sup> cells extracted from single-cell data of adult human retina.



Supplementary figure 4. Trajectory analysis of FVM-resident microglial subtypes

(A-B) Heatmap showing the upregulated genes along the pseudotime which were enriched for the GO terms associated with leukocyte migration and activation.

(C) Trajectory analysis of the 4 microglial subtypes identified in FVM-resident microglia which started from cycling MG and bifurcated into two cell fates, namely MG(1) and MG(3). Line chart showing the expression pattern of *MKI67*, *CX3CR1*, *MRC1* and *GPNMB* along the pseudotime.



Supplementary figure 5. The comparison of the scar-associated macrophage in liver fibrosis with FVM-resident microglia

(A) The integrated UMAP plot of CD45<sup>+</sup> cells from fibrotic liver and our data. The distribution of *AIF1* and *C1QA* expression in the separated UMAP.

(B) Violin plot showing that FVM-resident microglia expressed the higher level of scar-associated macrophage markers (*CD9*, *SPP1*) and extracellular matrix-associated genes (*FN1*, *SPARC*) than scar-associated macrophage identified in fibrotic liver.

(C) Heatmap of cluster marker genes of myeloid cells in the integrated UMAP.



Supplementary figure 6. The inferred signaling between cell types detected in FVM

(A) Dot plot showing the putative ligand-receptor signaling that was received by fibroblast.

(B) The inferred incoming communication patterns of target cells. which shows the correspondence between the inferred latent patterns of pathways and cell groups. The incoming signaling of fibroblast was marked red.

(C) The inferred outgoing communication patterns of secreting cells. The outgoing signaling of MG(1) was marked red.

(D) The inferred OSM, LIGHT and TWEAK signaling networks.

Cytokines	Ours (PDR/Ctrl (p value))	Suzuki Y et al <sup>23</sup> (PDR/Ctrl (p value))	Yu Y et al <sup>24</sup> (PDR/Ctrl (p value))	Xu Y et al <sup>25</sup> (PDR/Ctrl (p value))	Urbančič M et al <sup>26</sup> (PDR/Ctrl (p value))	Tsai T et al <sup>27</sup> (PDR/Ctrl (p value))
CTGF	177.01 (<0.0001)	NA	NA	NA	NA	NA
IL-6	41.28 (0.05)	8.03 (<0.01)	1.64 (0.009)	1.93 (0.0004)	NA	0.84 (0.51)
IL-8 (CXCL8)	37.12 (<0.0001)	12.6 (<0.01)	0.49 (0.465)	2.45 (<0.0001)	6.34 (0.0001)	NA
Angiopoietin- 2	17.11 (<0.0001)	NA	5.44 (0.047)	NA	NA	NA
PIGF	17.70 (0.006)	8.43 (0.12)	NA	NA	NA	384.2 (<0.001)
VEGF-A	14.22 (<0.0001)	31.33 (<0.01)	29.03 (0.016)	6.8 (<0.0001)	66.37 (0.0001)	247.68 (<0.001)
PDGF-DD	13.37 (0.018)	NA	NA	NA	NA	NA
MIP-1a (CCL3)	11.51 (0.012)	1.03 (>0.05)	NA	1.02 (0.940)	0.90 (0.31)	NA
Periostin	9.09(<0.0001)	NA	NA	NA	NA	NA
TGF-beta1	8.06 (<0.0001)	6.92 (0.249)	NA	NA	NA	NA
MMP-3	7.77 (0.002)	NA	NA	NA	NA	NA
IP-10 (CXCL10)	7.1 (0.02)	6.81 (<0.01)	0.85 (0.754)	1.72 (<0.0001)	NA	NA
MIP-1b (CCL4)	6.23 (0.026)	2.11 (<0.01)	NA	NA	NA	NA
MMP-1	5.79 (<0.0001)	1.21 (0.917)	NA	NA	NA	NA
MIF	5.01 (<0.0001)	NA	NA	NA	NA	NA
PDGF-BB	4.90 (0.004)	2.09 (<0.01)	2.15 (0.07)	NA	NA	NA
TNF-a	4.55 (<0.0001)	1.09 (>0.05)	NA	1.46 (0.163)	0.62 (0.25)	NA
MCP-1	4.54 (<0.0001)	3.23 (<0.01)	0.84 (0.028)	NA	4.31 (<0.0001)	NA
IFN-g	4.53 (<0.0001)	254.2 (>0.05)	NA	NA	NA	1.63 (0.04)
IL-1ra	4.43 (0.14)	1.48 (>0.05)	NA	NA	NA	NA
Eotaxin (CCL11)	4.4 (<0.001)	1.28 (>0.05)	NA	NA	NA	NA
IL-9	4.05 (<0.0001)	1.06 (>0.05)	NA	NA	NA	NA
TGF-beta3	4.04 (<0.0001)	0.78 (0.754)	NA	NA	NA	NA
CXCL9	3.89 (0.03)	NA	NA	2.0 (0.002)	NA	NA
IL-4	3.44 (<0.0001)	1.42 (0.917)	NA	NA	NA	NA
RANTES (CCL5)	3.28 (<0.0001)	1.57 (>0.05)	0.78 (0.834)	NA	NA	NA

Supplementary Table 1. Ratios between PDR and Ctrl of vitreous cytokines among reports

IL-10	3.27 (0.74)	1.57 (<0.05)		2.72 (<0.0001)	0.94 (0.02)	NA
IL-2	3.19 (0.001)	1.08 (>0.05)	NA	NA	NA	1.23 (0.62)
VEGF-C	2.46 (0.61)	NA	NA	NA	NA	NA
IL-17	2.45 (<0.001)	1.06 (>0.05)	NA	NA	NA	NA
IL-1β	2.4 (<0.0001)	1.23 (>0.05)	1.23 (0.917)	0.76 (0.46)	0.87 (0.51)	2.36 (0.02)
b-FGF	2.38 (<0.001)	0.94 (>0.05)	NA	NA	NA	NA
G-CSF	2.22 (0.01)	1.38 (>0.05)	0.71 (0.754)	NA	NA	NA
IL-12	1.75 (0.006)	1.38 (>0.05)	0.91 (0.60)	NA	0.79 (0.04)	NA
IL-7	1.31 (0.13)	1.28 (>0.05)	NA	NA	NA	NA
IL-18	1.22 (0.049)	NA	NA	2.29 (<0.0001)		NA
IL-13	0.44 (0.002)	1.96 (<0.01)	NA	NA	NA	NA

**PDR**: proliferative diabetic retinopathy; **Ctrl**: macular holes; **NA**: not available; **CTGF**: Connective tissue growth factor; **IL**: interleukin; **CXCL**: C-X-C chemokine ligand; **PIGF**: placental growth factor; **VEGF**: vascular endothelia growth factor; **PDGF**: Platelet derived growth factor; **MIP**: macrophage inflammatory protein; **TGF**: tissue growth factor; **MMP**: matrix metalloprotein; **IP-10**: interferon-inducible protein-10; **MIF**: macrophage-inhibiting factor; **TNF-a**: tumor necrosis factor-a; **MCP-1**: monocyte chemoattractant protein-1; **IFN-g**: interferon-g; **RANTES**: regulated upon activation normal T cell expressed and secreted; **b-FGF**: basic fibroblast growth factor; **G-CSF**: granulocyte-colony stimulating factor.

Number	Vision acuity (LogMAR)	Ophthalmic notes	Final vision acuity (LogMAR)	Follow-up (months)
CASE 1	2.9	Mild cataract, mild VH, FVM, TRD	2.9	13
CASE 2	2.0	Mild cataract, mild VH, FVM, TRD	0.52	12
CASE 3	1.0	FVM, TRD	1.0	11
CASE 4	1.22	FVM, TRD	0.52	6
CASE 5	1.30	Mild cataract, mild VH, FVM	0.1	5
CASE 6	1.0	VH, FVM	0.4	13
CASE 7	0.4	Mild cataract, cataract, mild VH, FVM	0.22	12
CASE 8	2.0	Cataract, mild VH, FVM	0.70	12
CASE 9	2.9	Dense VH, FVM	1.0	11
CASE 10	2.9	Mild cataract, FVM, TRD, previous PRP history	2.9	10
CASE 11	2.9	Cataract, FVM, TRD	1.52	2
CASE 12	2.9	FVM, TRD	0.7	2
CASE 13	2.9	FVM, TRD	1.0	3
CASE 14	2.9	VH, FVM	1.0	2
CASE 15	2.9	VH, FVM	0.60	2

Supplementary Table 2. Postoperative best corrected visual acuity of the included patients

**FVM**: fibrovascular membrane; **VH**: vitreous hemorrhage; **TRD**: tractional retinal detachment; **PRP**: pan-retinal photocoagulation.