

Supplementary Online Content

Analysis of inflammatory mediators in the vitreous humor of eyes with pan-uveitis according to aetiological classification

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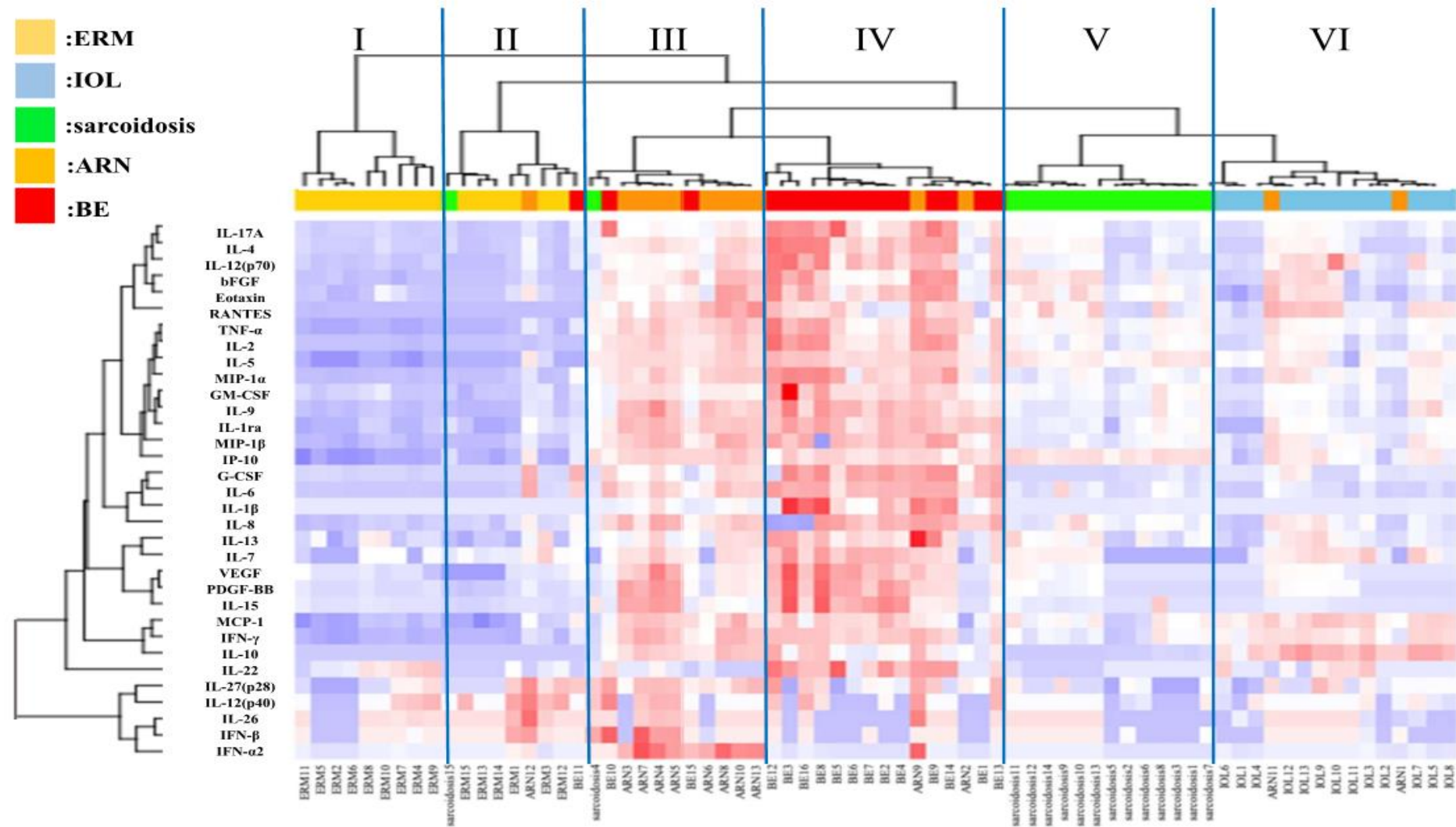
Supplementary Table S1. Patients' clinical details at the time of sample collection

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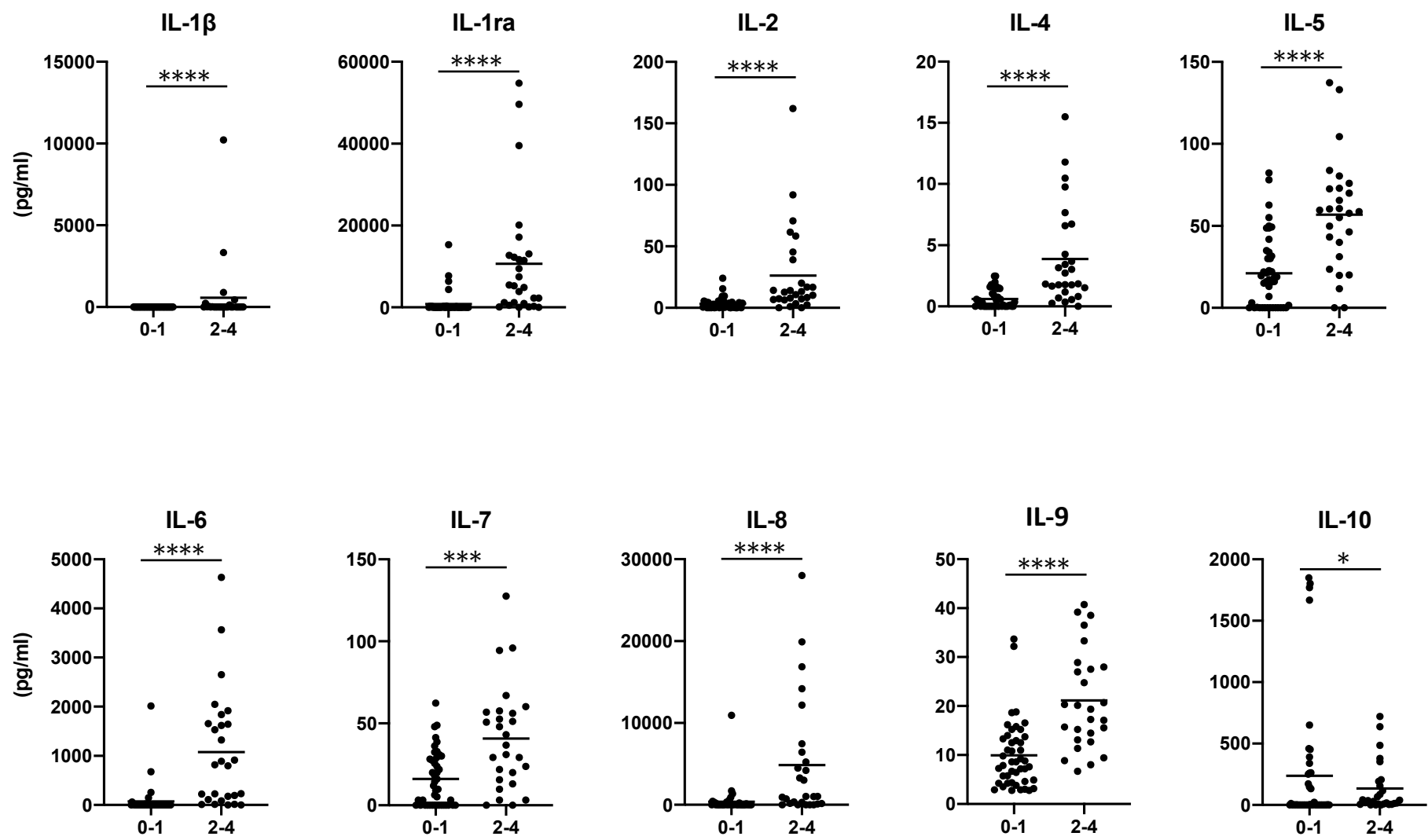
Supplementary Data S1. The raw data for patients' clinical details at the time of sample collection

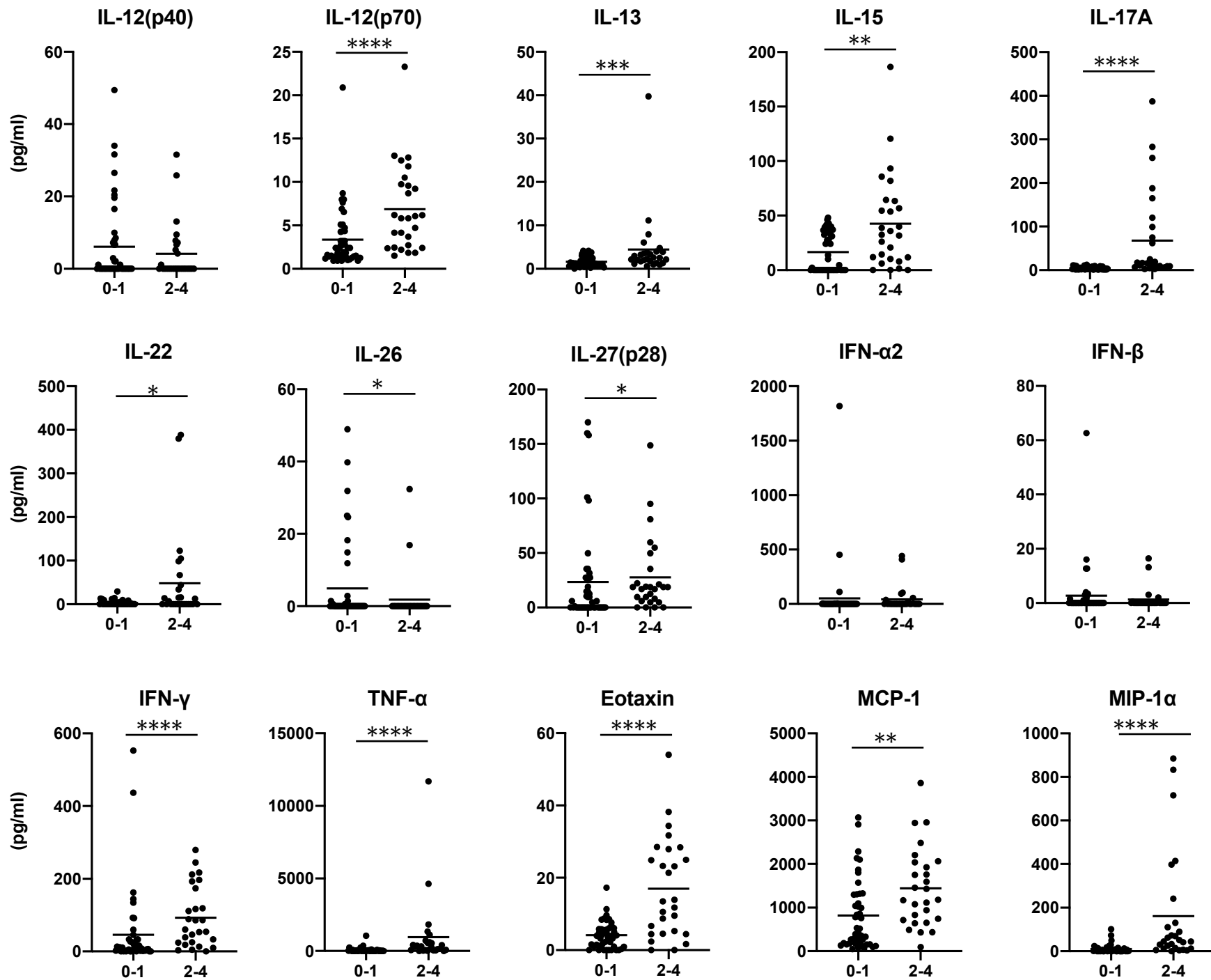
Supplementary Fig. S1. Heat map of inflammatory mediator concentrations in vitreous humor created using non-supervised hierarchical clustering. The mediator concentrations are depicted as colours ranging from blue to white to red, indicating low, intermediate, and high concentration, respectively, relative to the mean value for that cytokine. The label on the left of the heat map indicates cytokine expression. The disease entity associated with each sample is indicated by the label on the bottom as well as by the coloured bar on the top. The study eyes are separated in 6 main clusters (I to VI) separated by blue lines.

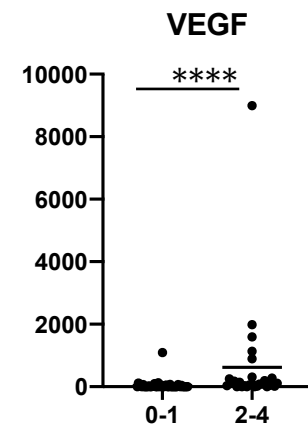
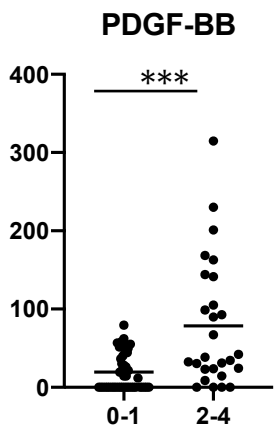
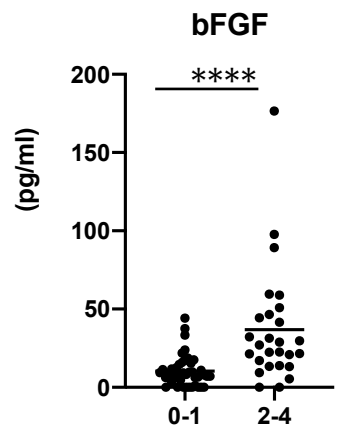
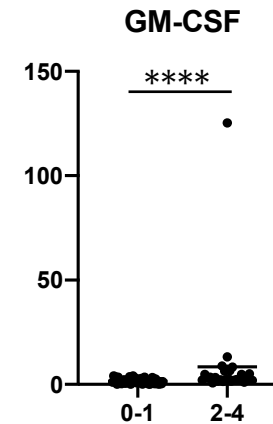
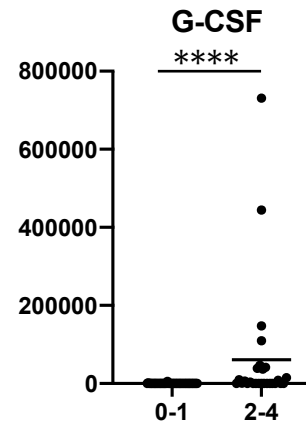
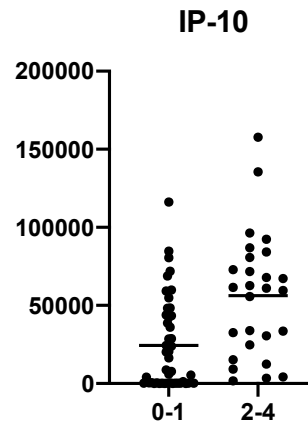
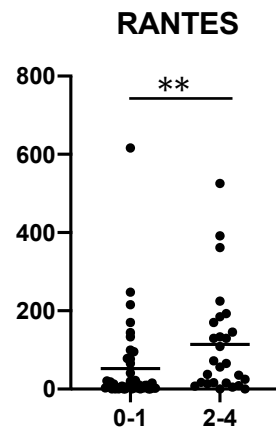
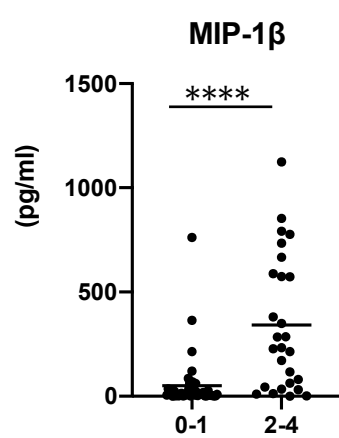
Supplementary Fig. S1



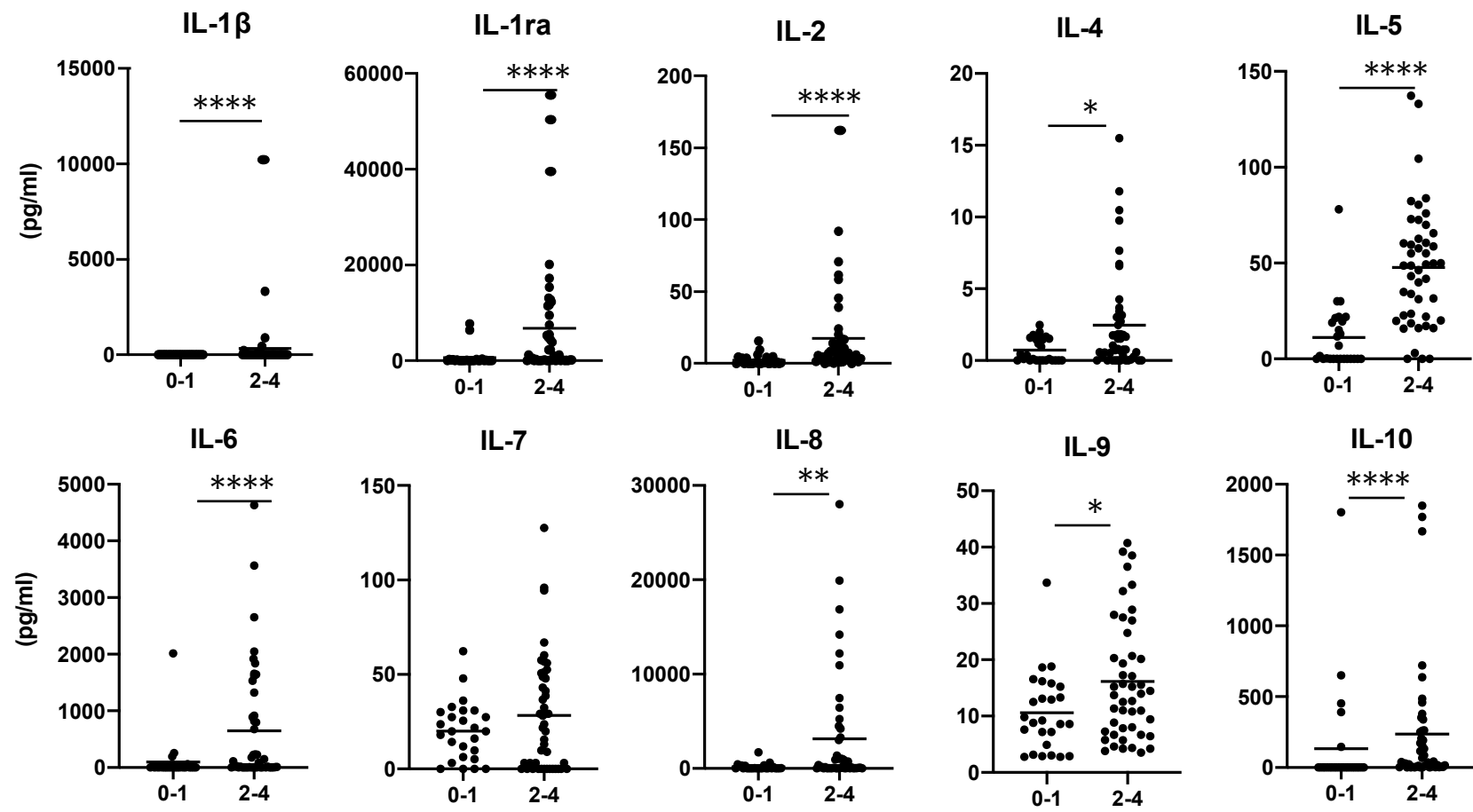
Supplementary Fig. S2. Comparisons of concentrations of immune mediators according to severity of intraocular inflammation in anterior chamber. The severity of intraocular inflammation in anterior chamber at the time of sample collection was determined using a semi-quantitative scoring system for cells in anterior chamber (0 to 4+) as described in the Patients and Methods. The eyes were divided according to the cells in the anterior chamber into a 0-1 cell group (1+ or less) and a 2-4 cell group (2+ or more), and the concentrations of 33 mediators were compared between the two groups. A p-value <0.05 was considered statistically significant. The p-values are shown in the upper portion of each graph. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

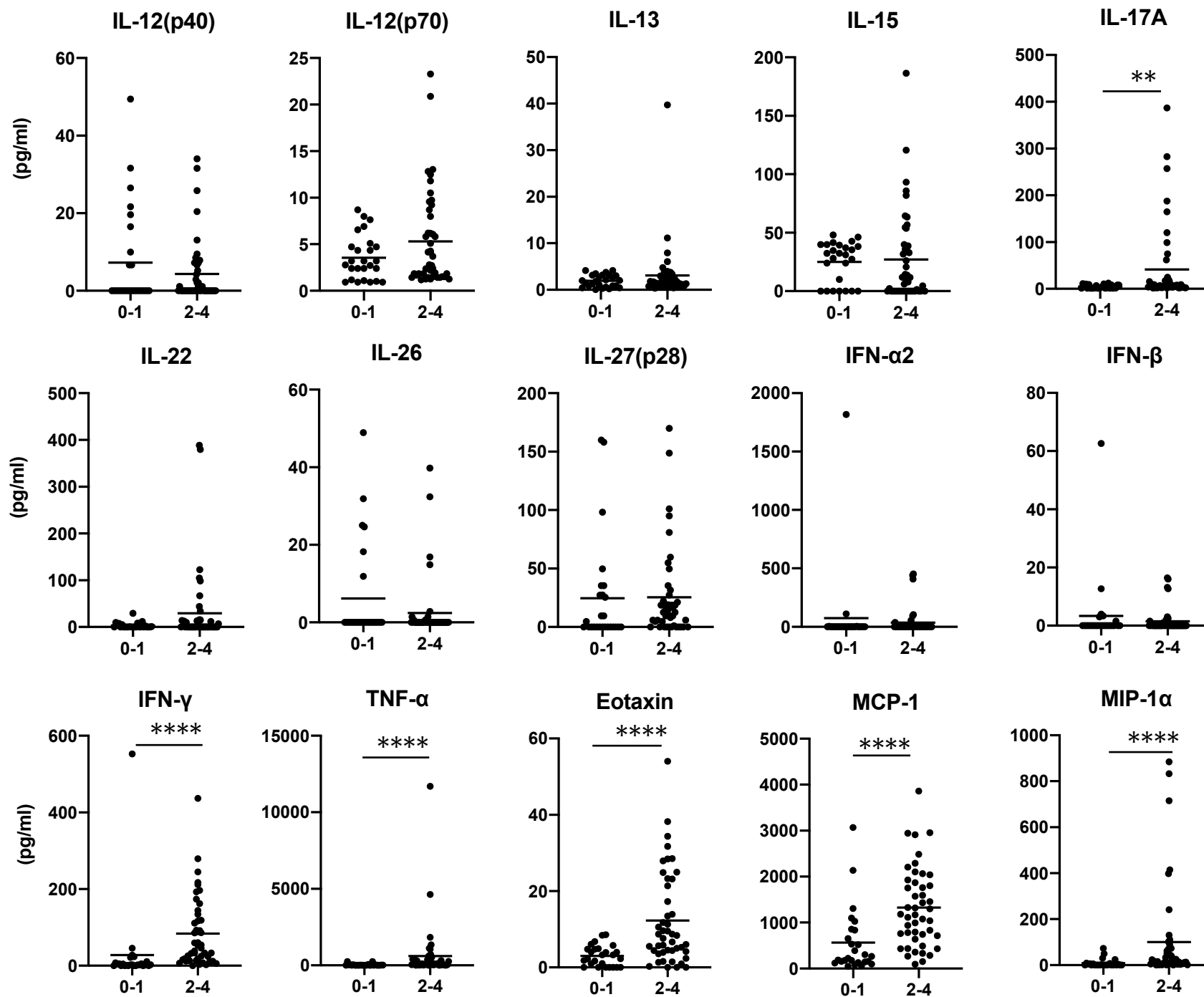


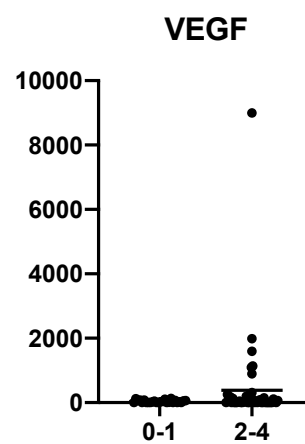
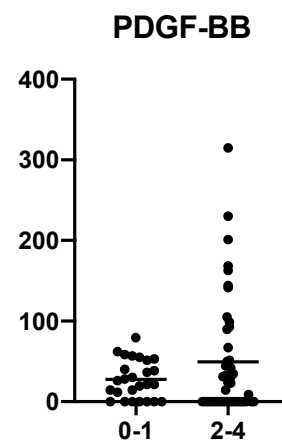
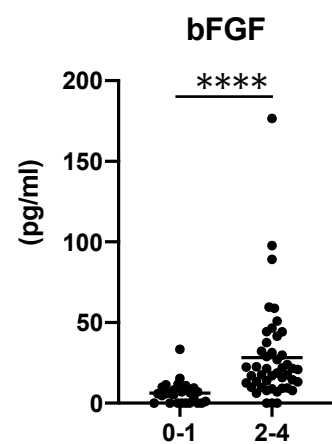
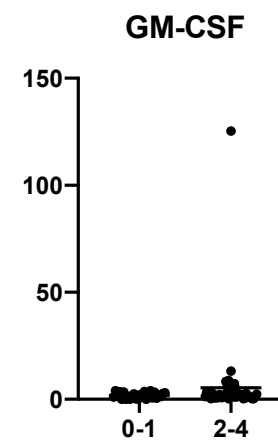
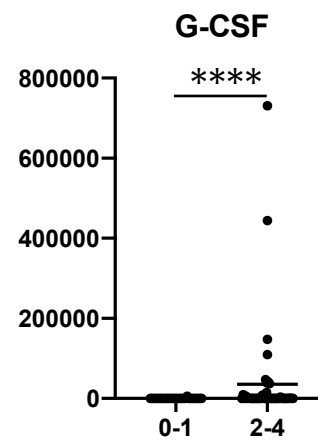
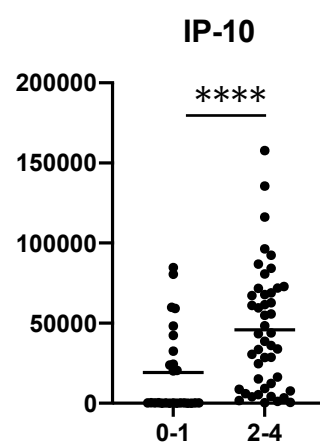
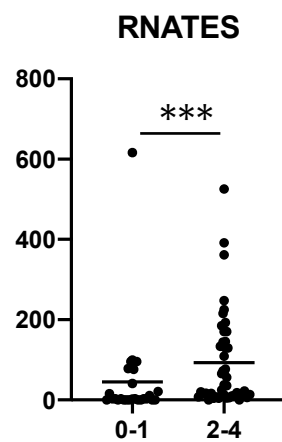
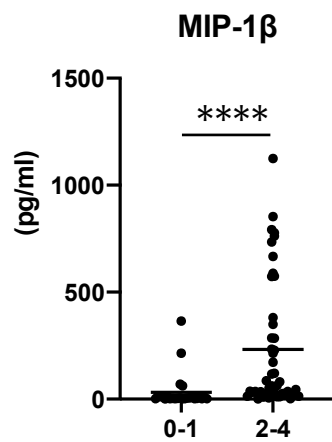




Supplementary Fig. S3. Comparisons of concentrations of immune mediators according to severity of vitreous haze. The severity of vitreous haze at the time of sample collection was determined using a semi-quantitative scoring system for vitreous haze (0 to 4+) as described in the Patients and Methods. The eyes were divided according to the vitreous haze (VH) into a VH 0-1 group (1+ or less) and a VH 2-4 group (2+ or more), and the concentrations of 33 mediators were compared between the two groups. A p-value <0.05 was considered statistically significant. The p-values are shown in the upper portion of each graph. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

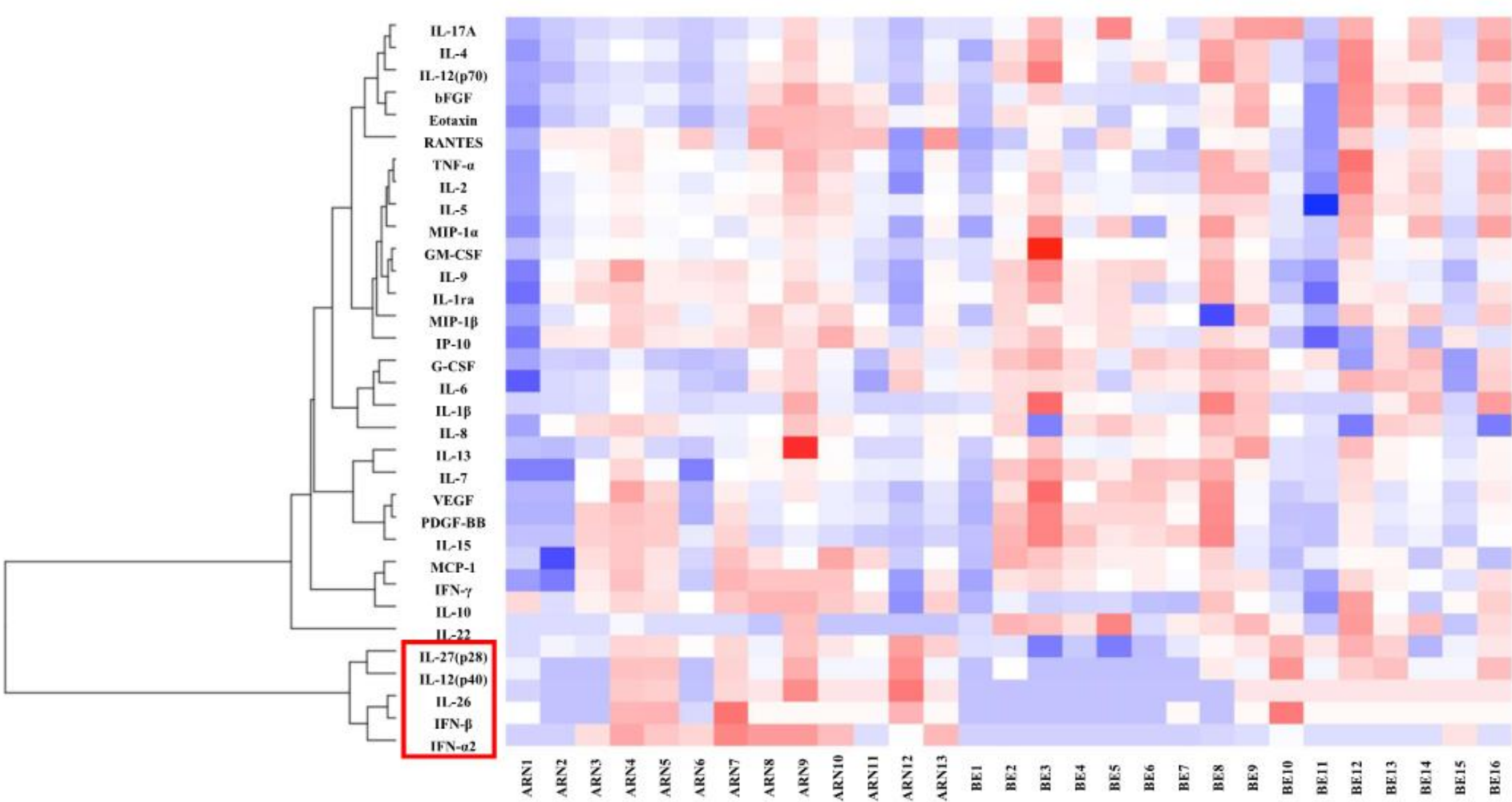






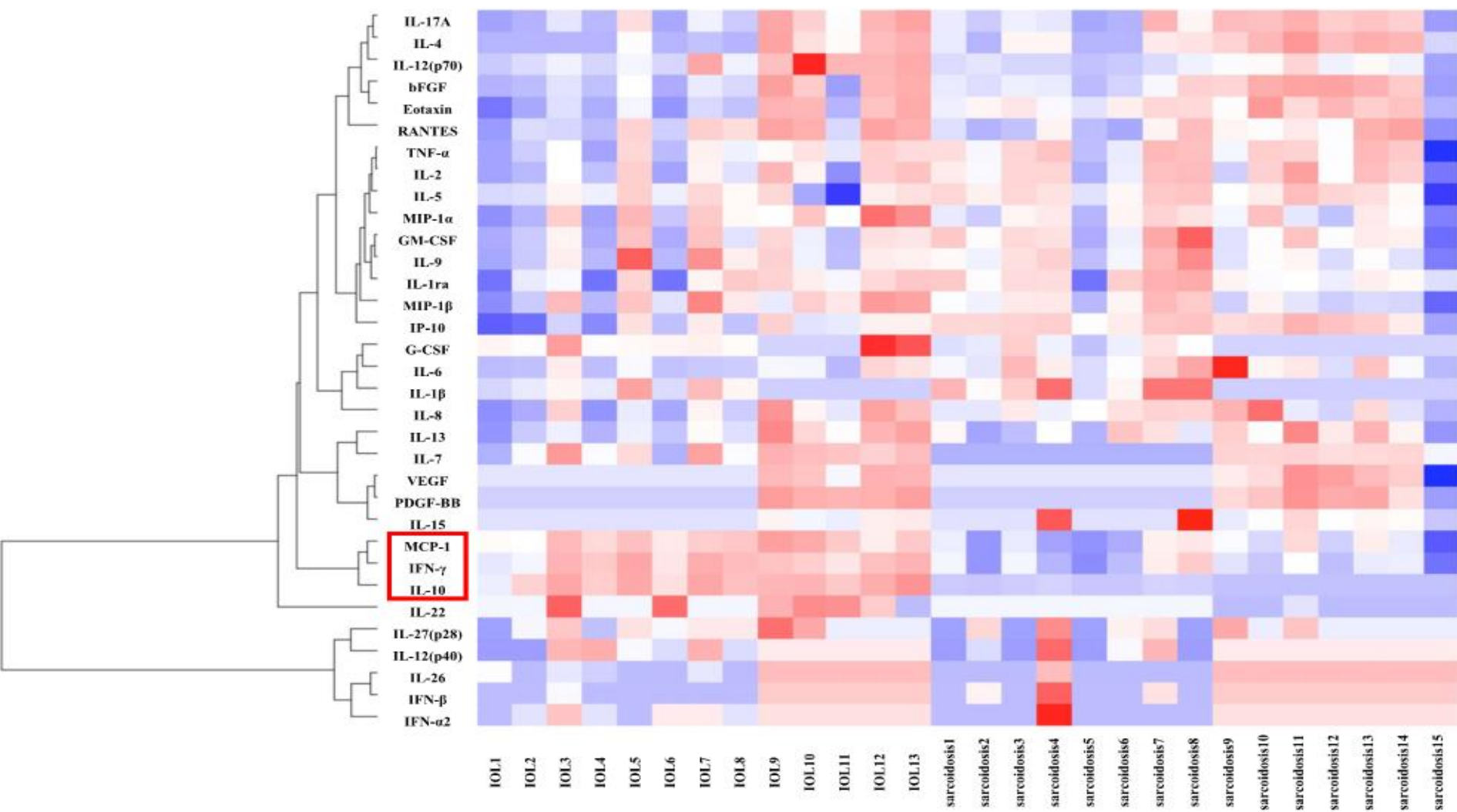
Supplementary Fig. S4. Heat map of inflammatory mediator concentrations in the vitreous humor in eyes with infectious uveitis (acute retinal necrosis and bacterial endophthalmitis) created using supervised hierarchical clustering with the x-axis fixed according to the disease components. The mediator is indicated by the label on the left. The cluster of cytokines with relatively higher expression in ARN are enclosed by the red line. ARN, acute retinal necrosis; BE, bacterial endophthalmitis

Supplementary Fig. S4

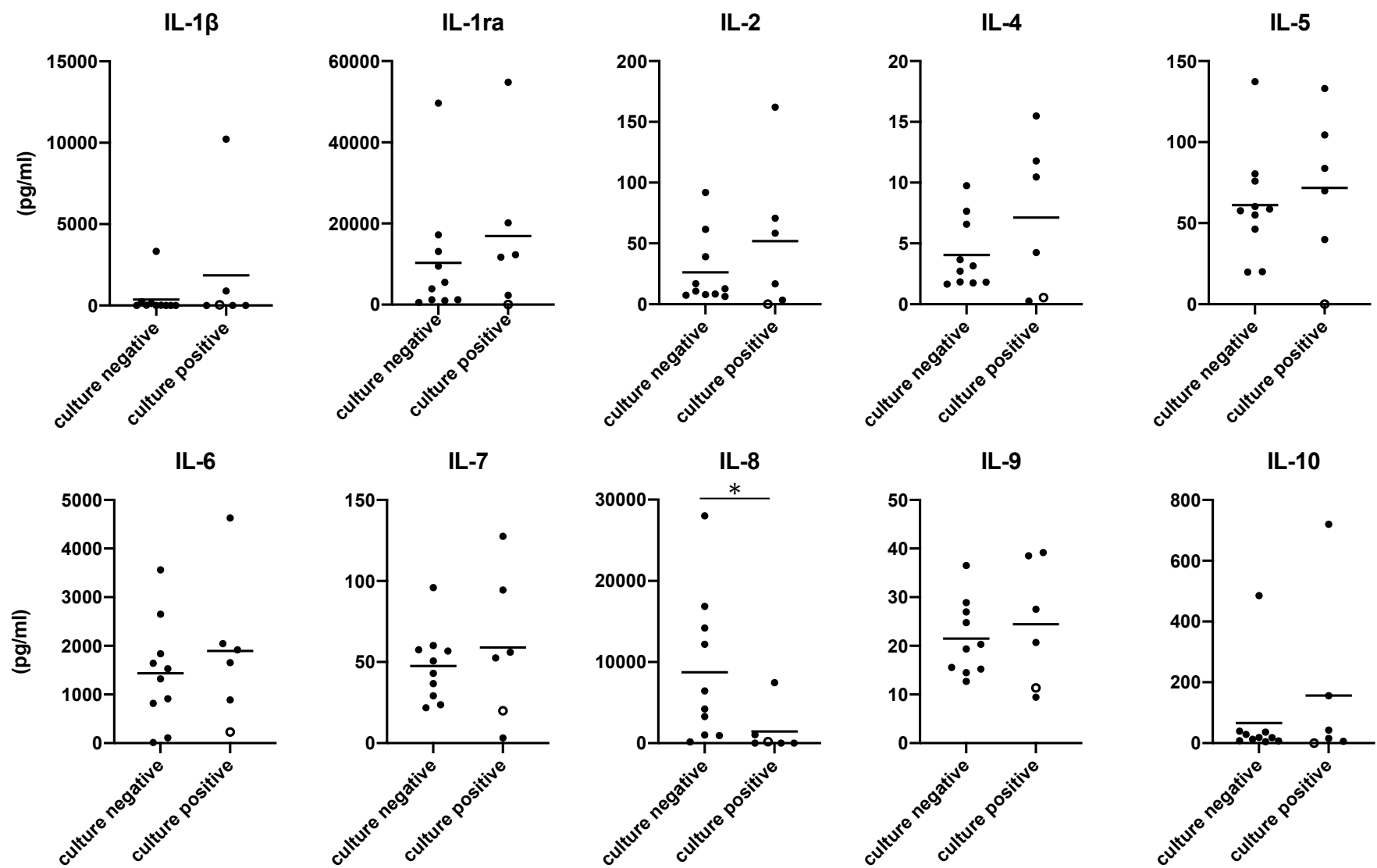


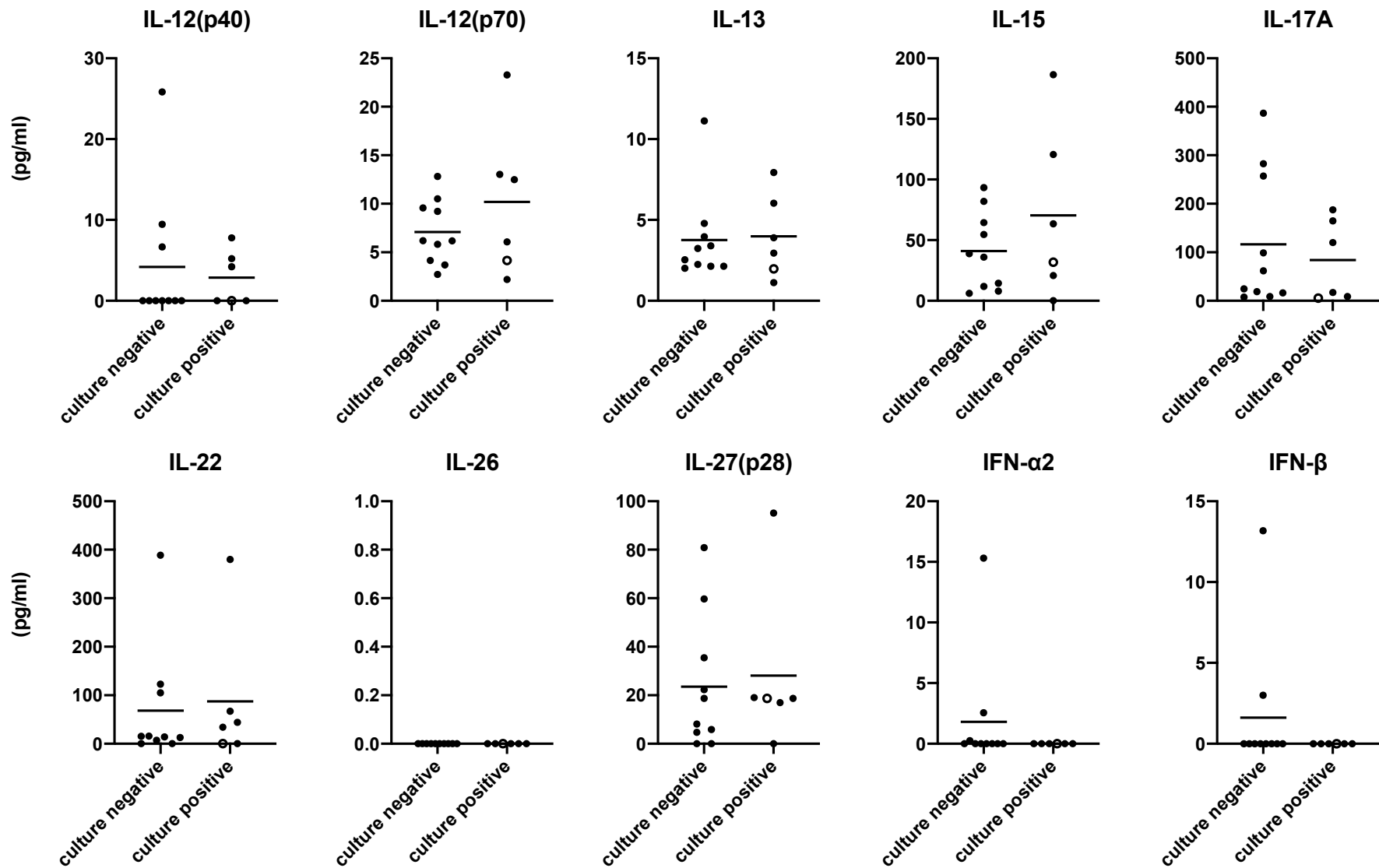
Supplementary Figure S5. Heat map of inflammatory mediator concentrations in the vitreous humor in eyes with non-infectious uveitis (intraocular lymphoma and sarcoidosis) created using supervised hierarchical clustering with the x-axis fixed according to the disease components. The mediator is indicated by the label on the left. The cluster of cytokines with relatively higher expression in IOL are enclosed by the red line. IOL, intraocular lymphoma

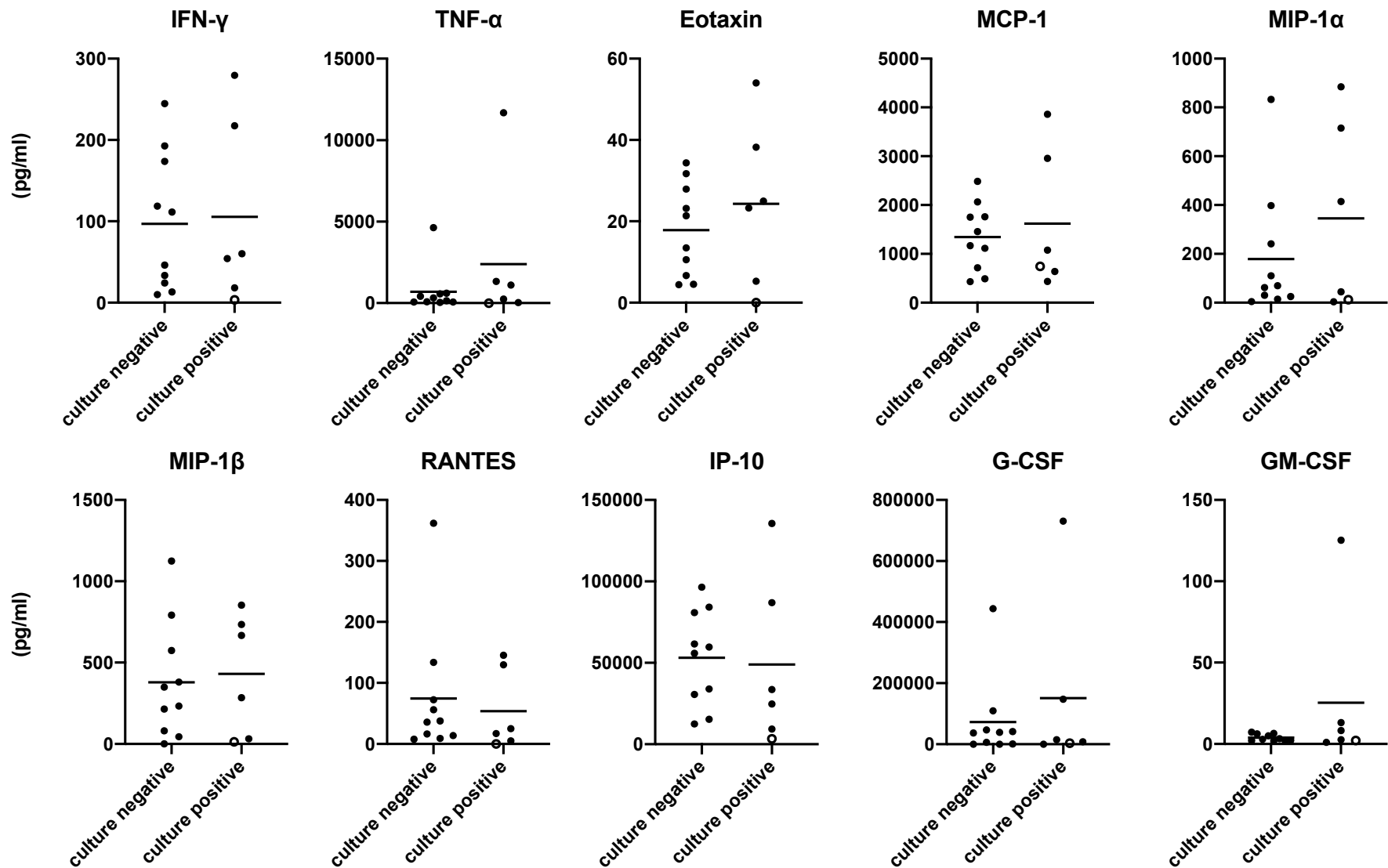
Supplementary Fig. S5

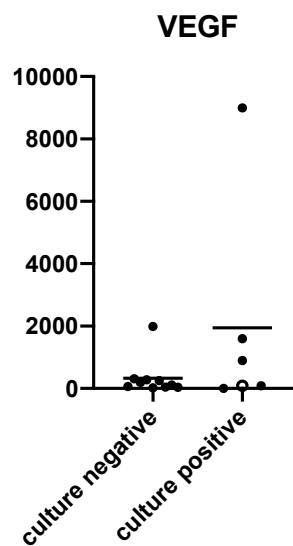
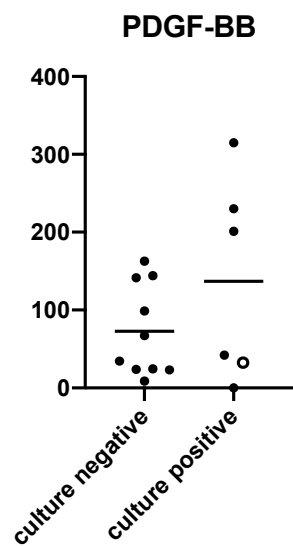
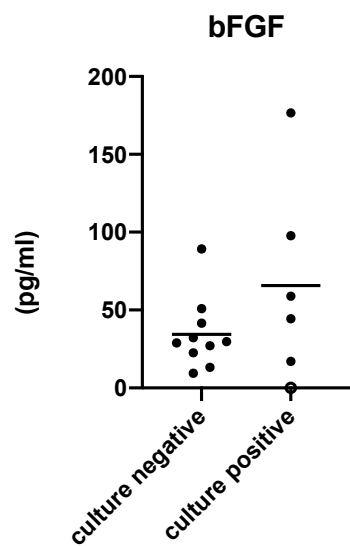


Supplementary Figure S6. Comparisons of concentrations of immune mediators according to culture-positive and culture-negative cases. The concentrations of 33 mediators were compared between **culture-positive and culture-negative cases in patients with bacterial endophthalmitis**. Open circles indicate cytokine concentrations in a case of bacterial endophthalmitis caused by Gram-negative bacteria. A p-value <0.05 was considered statistically significant.









Supplementary Table S1. Patients' clinical details at the time of sample collection

Diseases	ERM	IOL	sarcoidosis	ARN	BE
Timing of the vitrectomy from the onset of symptoms (months, mean $\pm$ SD)	unknown	10.82 $\pm$ 9.57	18.23 $\pm$ 22.64	0.62 $\pm$ 0.35	0.20 $\pm$ 0.20
Anterior inflammation score (mean $\pm$ SD)	0 $\pm$ 0	0.42 $\pm$ 0.64	0.9 $\pm$ 0.85	1.65 $\pm$ 0.80	3.56 $\pm$ 0.63
Vitreous opacity score (mean $\pm$ SD)	0 $\pm$ 0	2.08 $\pm$ 0.95	1.9 $\pm$ 0.93	2 $\pm$ 0.71	3.63 $\pm$ 0.62
Retinitis score (mean $\pm$ SD)	0 $\pm$ 0	0.54 $\pm$ 0.97	1 $\pm$ 0.85	2.46 $\pm$ 0.78	2.31 $\pm$ 1.14
Presence of hypopyon at the vitrectomy (cases, %)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (81.25%)
Systemic steroid use (cases, %)	0 (0%)	2 (15.38%)	5 (33.33%)	12 (92.31%)	1 (6.25%)
Steroid subconjunctival injection before surgery within 2 months (cases, %)	0 (0%)	0 (0%)	3 (20%)	1 (7.69%)	0 (0%)
Topical steroid eye drops (cases, %)	0 (0%)	4 (30.77%)	14 (93.33%)	13 (100%)	7 (43.75%)
Systemic antibiotic/antiviral agents (cases, %)	0 (0%)	0 (0%)	0 (0%)	12 (92.31%)	7 (43.75%)
Pseudophakic eyes at the vitrectomy (cases, %)	3 (20%)	6 (46.15%)	5 (33.33%)	0 (0%)	11 (68.75%)

ARN, acute retinal necrosis; BE, bacterial endophthalmitis; ERM, idiopathic epiretinal membrane; IOL, intraocular lymphoma; SD, standard deviation

Supplementary Table S2. Statistical data of immune mediators in vitreous humor of patients with ERM and other 4 uveitis diseases using Kruskal-Wallis test

Cytokines	p-values
IL-1 β	<.0001
IL-1ra	<.0001
IL-2	<.0001
IL-4	<.0001
IL-5	<.0001
IL-6	<.0001
IL-7	0.0001
IL-8	<.0001
IL-9	<.0001
IL-10	<.0001
IL-12(p40)	0.4725
IL-12(p70)	0.0001
IL-13	0.0003
IL-15	0.0175
IL-17A	<.0001
IL-22	<.0001
IL-26	0.0138
IL-27(p28)	0.0006
IFN- α 2	<.0001
IFN- β	0.101
IFN- γ	<.0001
TNF- α	<.0001
Eotaxin	<.0001
MCP-1	<.0001

MIP-1 α	<.0001
MIP-1 β	<.0001
RANTES	<.0001
IP-10	<.0001
G-CSF	<.0001
GM-CSF	<.0001
bFGF	<.0001
PDGF-BB	0.001
VEGF	<.0001

Significant differences (P < 0.05) are in bold.