

Supplementary Table S1. Comparisons of cytokine levels in culture supernatant of ARPE-19 cells incubated with aflibercept at various concentrations in the dark

A

4 groups	<i>p</i> value
IL-6	0.060
IL-8	0.051
IL-12	2.05 x 10⁻⁶
IL-17A	0.196
bFGF	0.119
MCP-1	0.418
VEGF	4.13 x 10⁻⁵

B

IL-12	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	3.87 x 10 ⁻⁷	3.87 x 10 ⁻⁷	3.87 x 10 ⁻⁷
31.3 µg-A	**	—	1.000	1.000
0.125 mg-A	**	—	—	1.000
0.50 mg-A	**	—	—	—

C

VEGF	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	1.03 x 10 ⁻⁴	8.61 x 10 ⁻⁵	8.12 x 10 ⁻⁵
31.3 µg-A	**	—	0.571	0.381
0.125 mg-A	**	—	—	0.967
0.50 mg-A	**	—	—	—

ARPE-19 cells were cultured with 7.81 µg/mL, 31.3 µg/mL, 0.125 mg/mL or 0.50 mg/mL of aflibercept in the dark. Four groups consisted of aflibercept-exposed cultures at indicated concentrations. (A) cytokine levels among the 4 groups were compared by non-repeated measures ANOVA. (B and C) *P* values in all pairwise comparisons of IL-12 and VEGF-A levels among aflibercept-exposed cultures were obtained by Tukey-Kramer test. *n* = 3 in each group. A: aflibercept, mg: mg/mL, µg: µg/mL.

Supplementary Table S2. Comparisons of cytokine levels in culture supernatant of ARPE-19 cells incubated with aflibercept at various concentrations under light irradiation

A

4 groups	<i>p</i> value
IL-6	0.015
IL-8	0.040
IL-12	0.479
IL-17A	0.734
bFGF	0.154
MCP-1	0.019
VEGF	0.046

B

IL-6	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.013	0.163	0.037
31.3 µg-A	*	—	0.095	0.489
0.125 mg-A			—	0.412
0.50 mg-A	*			—

C

IL-8	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.042	0.117	0.058
31.3 µg-A	*	—	0.650	0.974
0.125 mg-A			—	0.849
0.50 mg-A				—

D

MCP-1	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.035	0.085	0.018
31.3 µg-A	*	—	0.693	0.774
0.125 mg-A			—	0.292
0.50 mg-A	*			—

E

VEGF	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.148	4.97 x 10⁻²	0.061
31.3 µg-A		—	0.625	0.752
0.125 mg-A	*		—	0.993
0.50 mg-A				—

ARPE-19 cells were cultured with 7.81 $\mu\text{g/mL}$, 31.3 $\mu\text{g/mL}$, 0.125 mg/mL or 0.50 mg/mL of aflibercept under light irradiation. Four groups were composed of aflibercept-exposed cultures at indicated concentrations. **(A)** Cytokine levels among the 4 groups were compared. **(B to E)** All pairwise comparisons of IL-6, IL-8, MCP-1 and VEGF-A levels among aflibercept-exposed cultures were performed. $n = 3$ in each group.

Supplementary Table S3. Comparisons of cytokine levels in culture supernatant of ARPE-19 cells incubated with ranibizumab at various concentrations in the dark

A										
4 groups	p value				E					
IL-6	0.002				bFGF	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	
IL-8	0.013				1.95 µg-R	—	0.128	0.084	0.015	
IL-12	1.08 x 10 ⁻⁴				7.81 µg-R		—	0.960	0.152	
IL-17A	0.239				31.3 µg-R			—	0.240	
bFGF	0.021				0.125 mg-R	*			—	
MCP-1	0.005				F					
VEGF	8.22 x 10 ⁻⁵				IL-6	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	
B					MCP-1	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	
1.95 µg-R	—	0.006	0.007	0.001	1.95 µg-R	—	0.007	0.011	0.008	
7.81 µg-R	**	—	0.990	0.076	7.81 µg-R	**	—	0.828	0.996	
31.3 µg-R	**		—	0.059	31.3 µg-R	*		—	0.914	
0.125 mg-R	**			—	0.125 mg-R	**			—	
C					G					
IL-8	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	VEGF	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	
1.95 µg-R	—	0.702	0.143	0.012	1.95 µg-R	—	3.51 x 10 ⁻⁴	0.050	0.004	
7.81 µg-R		—	0.413	0.025	7.81 µg-R	**	—	0.001	8.59 x 10 ⁻⁵	
31.3 µg-R			—	0.097	31.3 µg-R		**	—	0.001	
0.125 mg-R	*	*		—	0.125 mg-R	**	**	**	—	
D										
IL-12	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R						
1.95 µg-R	—	0.021	0.102	2.71 x 10 ⁻⁴						
7.81 µg-R	*	—	0.004	1.14 x 10 ⁻⁴						
31.3 µg-R		**	—	0.001						
0.125 mg-R	**	**	**	—						

ARPE-19 cells were cultured with 1.95 µg/mL, 7.81 µg/mL, 31.3 µg/mL or 0.125 mg/mL of ranibizumab in the dark. Four groups consisted of ranibizumab-exposed cultures at indicated concentrations. (A) Cytokine levels among the 4 groups were compared. (B to G) All pairwise comparisons of IL-6, IL-8, IL-12, bFGF, MCP-1 and VEGF-A levels among ranibizumab-exposed cultures were performed. *n* = 3 in each group. R: ranibizumab.

Supplementary Table S4. Comparisons of cytokine levels in culture supernatant of ARPE-19 cells incubated with ranibizumab at various concentrations under light irradiation

A

4 groups	<i>p</i> value
IL-6	0.490
IL-8	0.325
IL-12	0.005
IL-17A	0.415
bFGF	0.632
MCP-1	0.105
VEGF	0.012

B

IL-12	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.739	0.045	0.005
31.3 µg-A		—	0.106	0.009
0.125 mg-A	*		—	0.080
0.50 mg-A	**	**		—

C

VEGF	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.809	0.047	0.014
31.3 µg-A		—	0.099	0.025
0.125 mg-A	*		—	0.416
0.50 mg-A	*	*		—

ARPE-19 cells were cultured with 1.95 µg/mL, 7.81 µg/mL, 31.3 µg/mL or 0.125 mg/mL of ranibizumab under light irradiation. Four groups were composed of ranibizumab-exposed cultures at indicated concentrations. (A) Cytokine levels among the 4 groups were compared. (B and C) All pairwise comparisons of IL-12 and VEGF-A levels among ranibizumab-exposed cultures were performed. *n* = 3 in each group.