

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

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

  

<b>B</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 <sup>-7</sup>	3.87 x 10 <sup>-7</sup>	3.87 x 10 <sup>-7</sup>
31.3 µg-A	**	—	1.000	1.000
0.125 mg-A	**		—	1.000
0.50 mg-A	**			—

  

<b>C</b>				
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 <sup>-4</sup>	8.61 x 10 <sup>-5</sup>	8.12 x 10 <sup>-5</sup>
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**

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

  

<b>B</b>				
IL-6	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	<b>0.013</b>	0.163	<b>0.037</b>
31.3 µg-A	*	—	0.095	0.489
0.125 mg-A			—	0.412
0.50 mg-A	*			—

  

<b>C</b>				
IL-8	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	<b>0.042</b>	0.117	0.058
31.3 µg-A	*	—	0.650	0.974
0.125 mg-A			—	0.849
0.50 mg-A				—

  

<b>D</b>				
MCP-1	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	<b>0.035</b>	0.085	<b>0.018</b>
31.3 µg-A	*	—	0.693	0.774
0.125 mg-A			—	0.292
0.50 mg-A	*			—

  

<b>E</b>				
VEGF	7.81 µg-A	31.3 µg-A	0.125 mg-A	0.50 mg-A
7.81 µg-A	—	0.148	<b>4.97 x 10<sup>-2</sup></b>	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 µg/mL, 31.3 µg/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	<i>p</i> value								
IL-6	0.002								
IL-8	0.013								
IL-12	1.08 x 10 <sup>-4</sup>								
IL-17A	0.239								
bFGF	0.021								
MCP-1	0.005								
VEGF	8.22 x 10 <sup>-5</sup>								
B									
IL-6	1.95 µg-R	7.81 µg-R	31.3 µg-R	0.125 mg-R	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									
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 <sup>-4</sup>	0.050	0.004
7.81 µg-R		—	0.413	0.025	7.81 µg-R	**	—	0.001	8.59 x 10 <sup>-5</sup>
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 <sup>-4</sup>					
7.81 µg-R	*	—	0.004	1.14 x 10 <sup>-4</sup>					
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
<b>IL-12</b>	<b>0.005</b>
IL-17A	0.415
bFGF	0.632
MCP-1	0.105
<b>VEGF</b>	<b>0.012</b>

**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	<b>0.045</b>	<b>0.005</b>
31.3 µg-A		—	0.106	<b>0.009</b>
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	<b>0.047</b>	<b>0.014</b>
31.3 µg-A		—	0.099	<b>0.025</b>
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.