

Supplementary Materials for

**Neuroinflammation as a cause of differential Müller cell regenerative responses to retinal injury**

Diana García-García *et al.*

Corresponding author: Muriel Perron, muriel.perron@universite-paris-saclay.fr

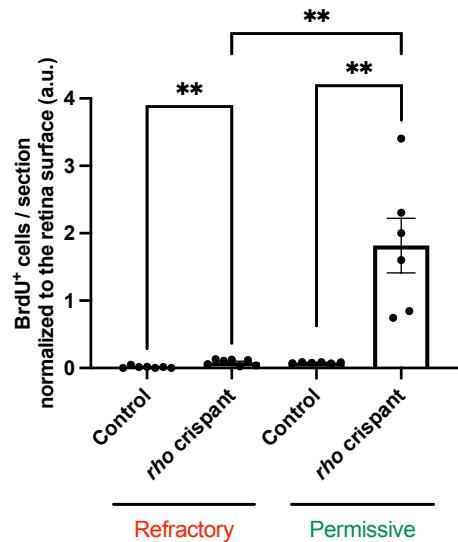
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Tables S1 to S5

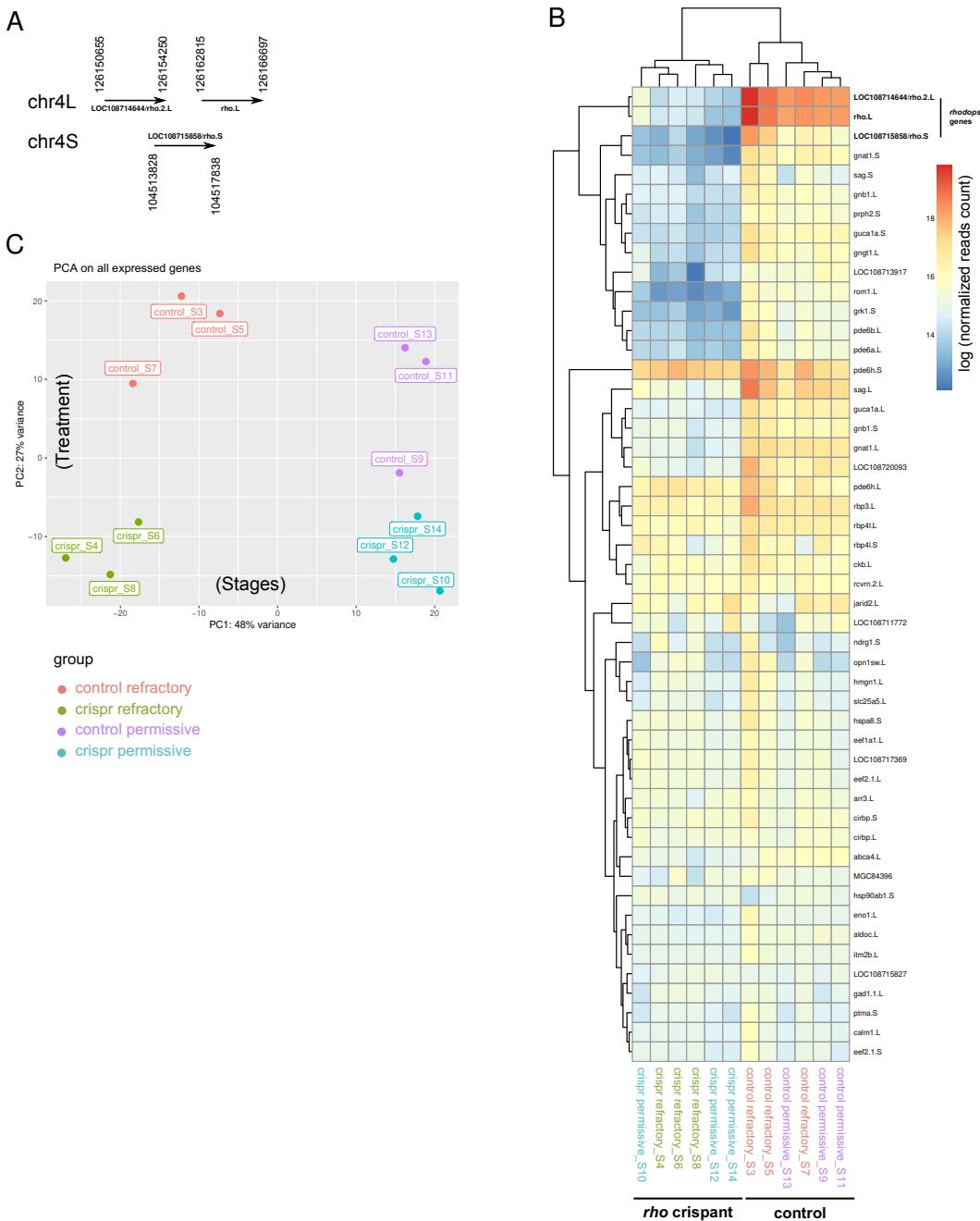
## Supplementary Materials

Figure S1



**Figure S1. The response of Müller cells to injury varies along with aging in *Xenopus* tadpoles.** Quantification of BrdU-positive cells (3-day exposure) in retinal sections of young (refractory) or old (permissive) control and *rho* crispant tadpoles. Data were normalized to the entire surface of the retinal section and are represented as mean  $\pm$  SEM. Each point represents one retina. \*\* $p < 0.01$  (Mann-Whitney test).

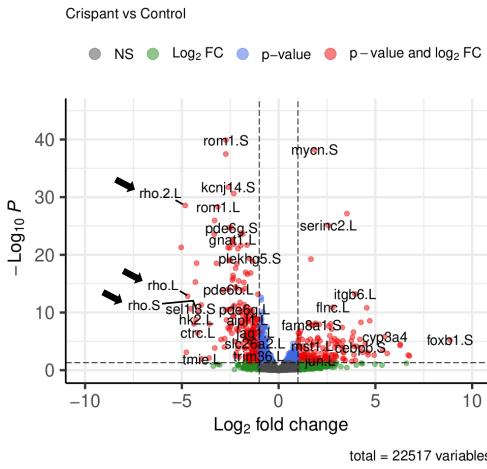
**Figure S2**



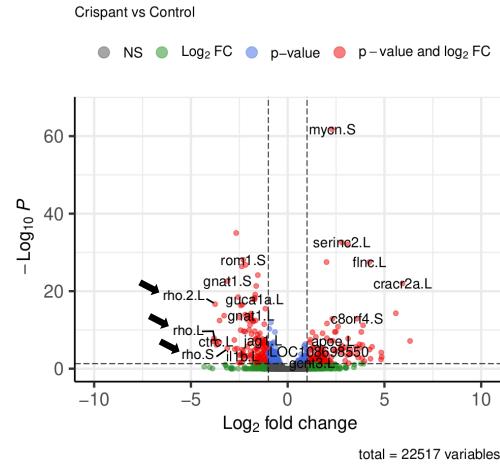
**Figure S2. Mapping data.** Following adapter trimming, the RNAseq data were mapped to *Xenopus laevis* genome 9.2 and uniquely mapped reads were assigned to genes using the annotation available on Xenbase. **(A)** Chromosomal locations of the three *rho* loci targeted by CRISPR/Cas9. **(B)** Clustered heatmap of the 50 most expressed genes of the RNAseq dataset. It highlights the clear separation between *rho*-cristant and control tadpoles. **(C)** Principal component analysis (PCA) on expressed genes of the RNAseq dataset. PC1 (48%) is most likely associated with the developmental stage of the tadpoles, while PC2 (27%) is most likely associated with the treatment condition. Components 1 and 2 explain together 75 % of the variance.

**Figure S3**

**A Refractory stage**

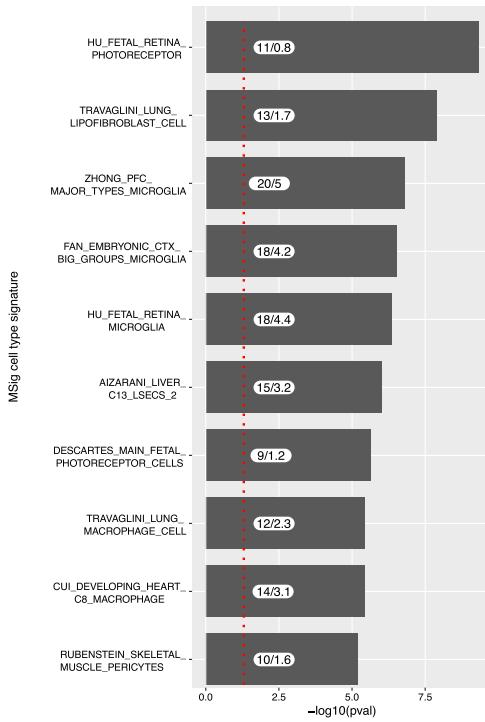


**Permissive stage**



**B**

**Refractory stage**

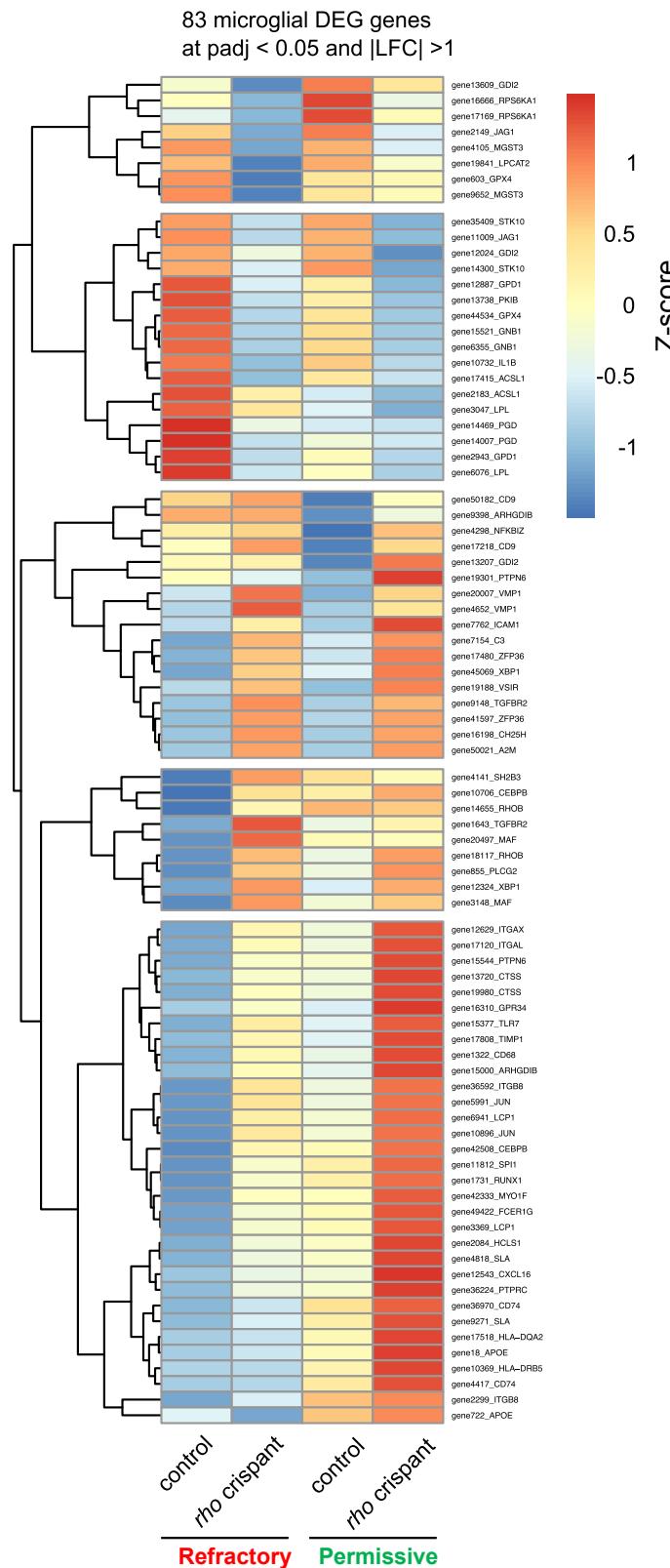


**Permissive stage**



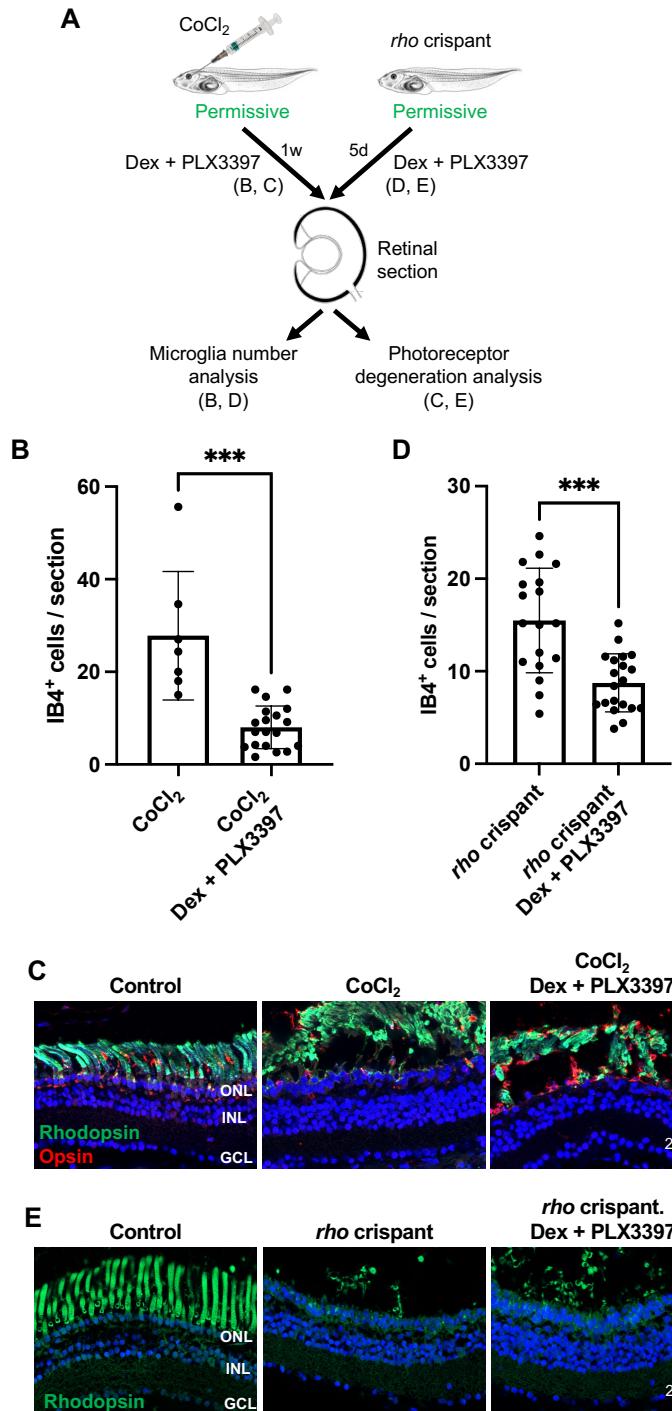
**Figure S3. Differential gene expression at refractory and permissive stages.** **(A)** Volcano plot representing differentially expressed genes at refractory and permissive stages. 456 and 272 genes are statistically differentially expressed ( $|LFC| > 1$ ,  $p_{adj} < 0.05$ ) at refractory and permissive stages, respectively. Arrows point to *rho* genes targeted by CRISPR/Cas9. **(B)** Enriched cell-type molecular signature identified based on the differentially expressed genes ( $|LFC| > 1$  and  $p_{adj} < 0.05$ ). Numbers in bars represent observed/expected genes.

**Figure S4**

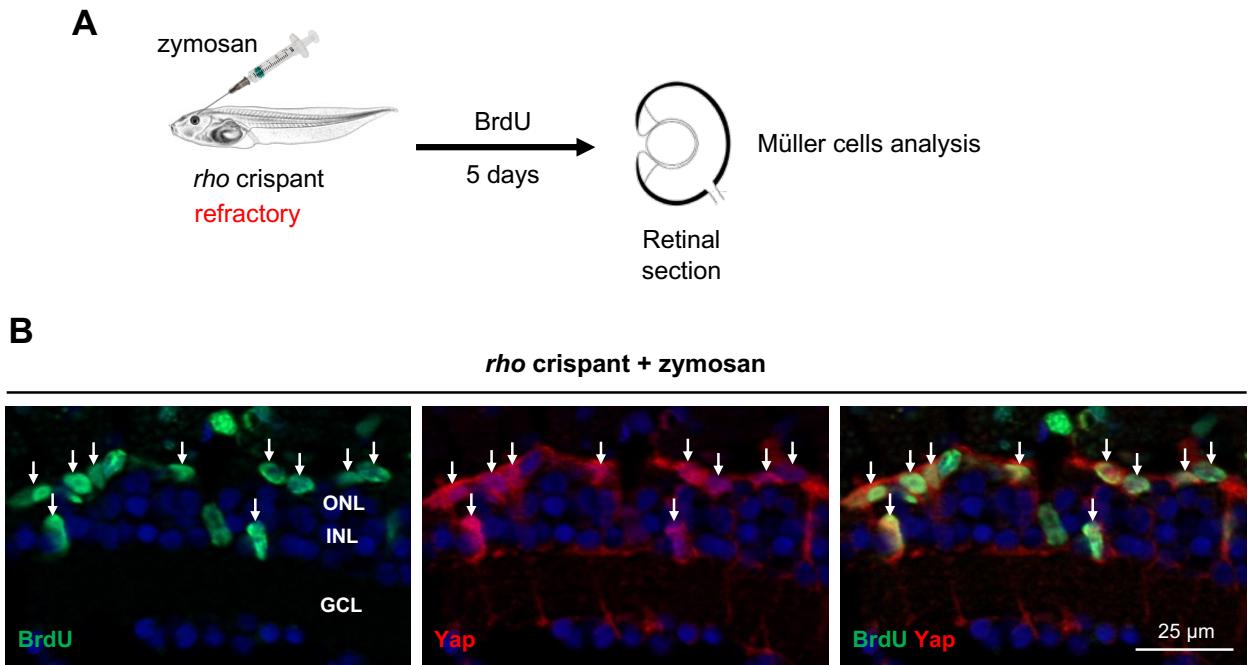


**Figure S4. Heatmap of differentially expressed genes.** Clustered heatmap of differentially expressed genes belonging to the microglia molecular signature. Enlargement of the cluster of interest is shown in **Fig. 1D**.

**Figure S5**

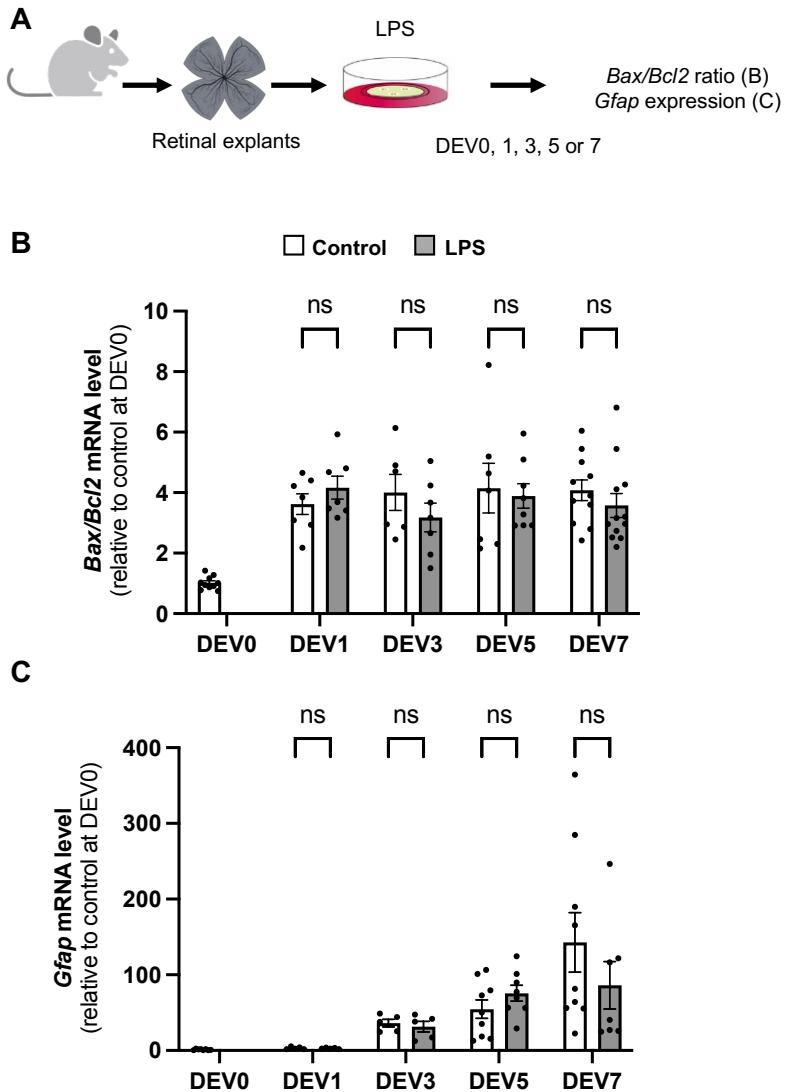


**Figure S5. Dex plus PLX3397 treatment efficiently decreases the number of microglial cells in CoCl<sub>2</sub>-injected or *rho* crispant tadpoles, without impacting retinal degeneration.** (A) Outline of the experimental procedure used in (B-E). Stage 56/62 (permissive stage) CoCl<sub>2</sub>-injected (B, C) or *rho* crispant (D, E) tadpoles were soaked in PLX3397 plus Dex solution for 5 days (5d) or 1 week (1w) as indicated, starting one day before CoCl<sub>2</sub> injection. They were then processed for immunolabeling on retinal sections. (B, D) Quantification of IB4-positive cells (microglia). (C, E) Representative images of retinal sections labeled for Opsins (cones) and/or Rhodopsin (rods). Nuclei are counterstained with Hoechst. Data are represented as mean ± SEM, and each point represents one retina. \*\*\*P < 0.001 (Mann-Whitney test). GCL, ganglion cell layer; INL, inner nuclear layer; ONL, outer nuclear layer.



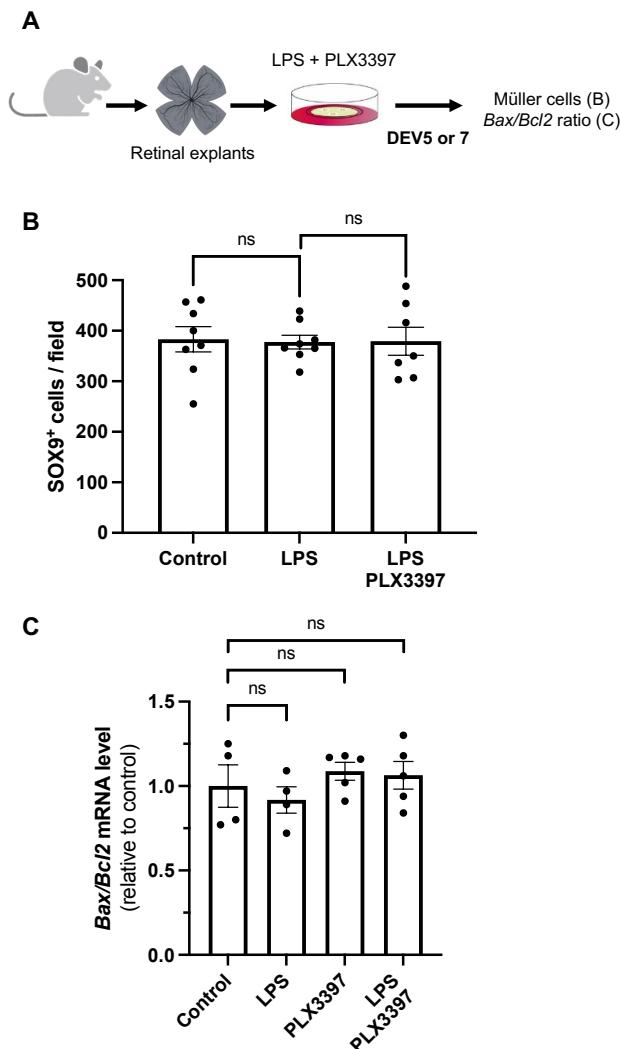
**Figure S6. Proliferative cells upon zymosan injection at the refractory stage are Müller cells.** **(A)** Outline of the experimental procedure used in (B). Stage 48/49 (refractory) *rho* crispant tadpoles were intraocularly injected with zymosan and then exposed to BrdU solution for 5 days before being processed for immunolabeling on retinal sections. **(B)** Representative images of retinal sections co-labeled for BrdU and Yap. Arrows point to double-labeled cells. GCL, ganglion cell layer; INL, inner nuclear layer; ONL, outer nuclear layer.

**Figure S7**



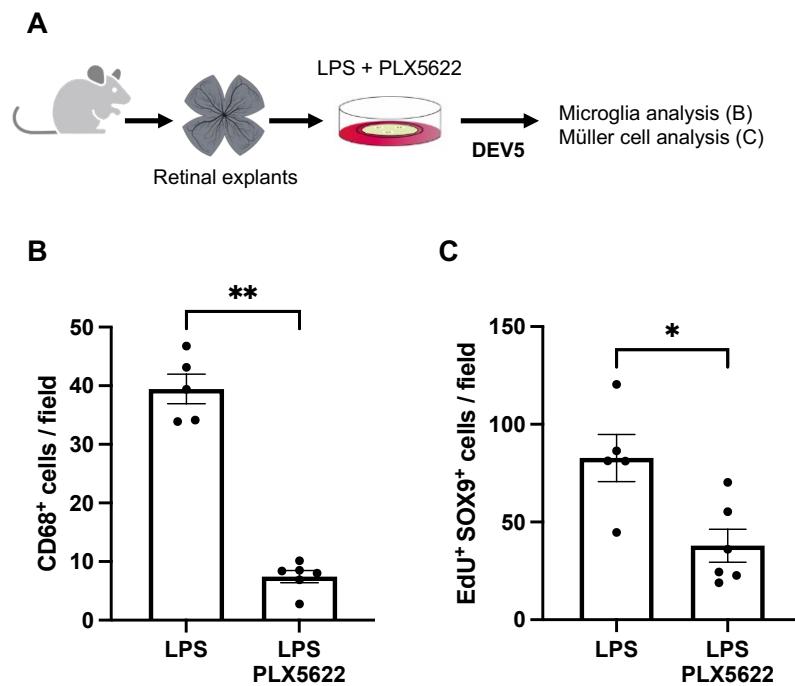
**Figure S7. Absence of toxicity of LPS on retinal cells in mouse explants.** (A) Outline of the experimental procedure used in (B, C). Retinas from wild-type mice were flattened and cultured for up to 7 days in the presence of LPS. They were then processed for qPCR analysis. (B, C) qPCR analysis of *Bax/Bcl2* expression ratio (B) or *Gfap* expression (C) in control and LPS-treated retinal explants at different culture time points relative to uncultured control condition (DEV0). Data are represented as mean  $\pm$  SEM, and each point represents one retinal explant. ns: non-significant (Mann-Whitney test).

**Figure S8**



**Figure S8. Impact of LPS plus PLX3397 treatment on the survival of mouse Müller glial cells.** (A) Outline of the experimental procedure used in (B, C). Retinas from wild-type mice were flattened and cultured in the presence of LPS, PLX3397 or LPS plus PLX3397. Retinal explants were processed for immunostaining analysis at DEV7 (B) or processed for qPCR analysis at DEV5 (C). (B) Quantification of SOX9-positive cells (Müller cells). (C) Retinal qPCR analysis of *Bax/Bcl2* expression ratio. Data are represented as mean  $\pm$  SEM, and each point represents one retinal explant. ns: non-significant (Mann-Whitney test).

**Figure S9**



**Figure S9. PLX5622 counteracts the LPS-driven proliferation of Müller glial cells in mouse retinal explants.** (A) Outline of the experimental procedure used in (B, C). Retinas from wild-type mice were flattened and cultured for 5 days in the presence of EdU plus LPS, or plus LPS and PLX5622. Retinal explants were processed for immunostaining analysis at DEV5. (B, C) Quantification of CD68-positive cells (activated microglia, B) or double EdU- and SOX9-positive cells (proliferative Müller cells, C) in LPS or LPS plus PLX5622-treated retinal explants. Data are represented as mean  $\pm$  SEM, and each point represents one retinal explant. \* $P < 0.05$ , \*\* $P < 0.01$  (Mann-Whitney test).

**Supplementary Table S1.**

**Refractory Stage**

ID	Description	setSize	Enrichment Score	Normalized Enrichment Score	pvalue	p.adjust	qvalue
GO:0009583	Detection of light stimulus	45	-0,82	-2,98	1,00E-15	4,96E-13	3,23E-13
GO:0019646	Aerobic electron transport chain	66	-0,75	-2,95	1,00E-15	4,96E-13	3,23E-13
GO:0009584	<u>Detection of visible light</u>	36	-0,85	-2,92	1,00E-15	4,96E-13	3,23E-13
GO:0042773	ATP synthesis coupled electron transport	71	-0,72	-2,89	1,00E-15	4,96E-13	3,23E-13
GO:0042775	Mitochondrial ATP synthesis coupled electron transport	71	-0,72	-2,89	1,00E-15	4,96E-13	3,23E-13
GO:0022904	Respiratory electron transport chain	88	-0,69	-2,83	1,00E-15	4,96E-13	3,23E-13
GO:0002521	<b>Leukocyte differentiation</b>	339	0,47	2,40	1,02E-15	4,96E-13	3,23E-13
GO:0048858	Cell projection morphogenesis	453	0,44	2,28	3,63E-15	1,38E-12	8,98E-13
GO:0032990	Cell part morphogenesis	469	0,43	2,25	3,57E-15	1,38E-12	8,98E-13
GO:0002088	<u>Lens development in camera-type eye</u>	61	0,76	2,97	4,64E-15	1,59E-12	1,03E-12

**Permissive Stage**

ID	Description	setSize	Enrichment Score	Normalized Enrichment Score	pvalue	p.adjust	qvalue
GO:0050776	<b>Regulation of immune response</b>	382	0,59	2,14	2,74E-15	9,37E-12	7,46E-12
GO:0002684	<b>Positive regulation of immune system process</b>	465	0,56	2,05	1,11E-13	1,90E-10	1,51E-10
GO:0009583	<u>Detection of light stimulus</u>	45	-0,86	-2,61	1,15E-12	1,31E-09	1,05E-09
GO:0045087	<b>Innate immune response</b>	343	0,59	2,10	2,95E-12	2,17E-09	1,73E-09
GO:0045321	Leukocyte activation	463	0,54	1,99	3,17E-12	2,17E-09	1,73E-09
GO:0098542	<b>Defense response to other organism</b>	442	0,54	1,99	7,51E-12	4,28E-09	3,41E-09
GO:0009584	<u>Detection of visible light</u>	36	-0,87	-2,56	1,53E-11	7,46E-09	5,94E-09
GO:0042110	<b>T cell activation</b>	260	0,61	2,13	2,39E-11	1,02E-08	8,14E-09
GO:0007602	Phototransduction	33	-0,87	-2,53	4,39E-11	1,67E-08	1,33E-08
GO:0002263	<b>Cell activation involved in immune response</b>	138	0,69	2,25	5,61E-11	1,92E-08	1,53E-08

**Table S1. GSEA top 5 most enriched or depleted biological processes at refractory or permissive stages between *rho* crisprants and control retinas.** Log2FC ranked gene list from differential analysis performed at refractory or permissive stages. Biological processes pertaining to the visual system are underlined and biological processes pertaining to inflammatory response are in bold.

**Supplementary Table S2.**

**Primary antibodies and lectin used in *Xenopus***

Antigen	Host species	Distributor	Reference	Dilution
BrdU	Rat	Abcam	ab6326	1/400
BrdU	Mouse	Becton Dickinson	347580	1/100
Isolectin B4 – Alexa Fluor 594 Conjugate		Thermo Fisher Sc.	I21413	1/500
S-Opsin	Rabbit	Millipore	AB5407	1/500
M-Opsin	Rabbit	Millipore	AB5405	1/500
PCNA	Mouse	DAKO	M0879	1/500
Rhodopsin	Mouse	Millipore	MABN15	1/1000
Yap	Rabbit	Abcam	ab52771	1/50

**Primary antibodies used in mice**

Antigen	Host species	Distributor	Reference	Dilution
CD68	Rat	Bio-Rad	MCA1957GA	1/300
SOX9	Rabbit	Abcam	ab185966	1/300

**Secondary antibodies**

Antibody	Host	Company	Reference	Dilution
Anti-mouse IgG, Alexa 488	Goat	ThermoFisher Sc.	A-11001	1/1000
Anti-rabbit IgG, Alexa 555	Goat	ThermoFisher Sc.	A-21428	1/1000
Anti-rat IgG, Alexa 555	Goat	ThermoFisher Sc.	A-21434	1/1000
Anti-rat IgG, Alexa 647	Goat	ThermoFisher Sc.	A-21247	1/500

**Table S2. List of antibodies.**

**Supplementary Table S3.**

**Primers for qPCR (*Xenopus*)**

Target	Forward (5'-3')	Reverse (5'-3')
<i>anxA1</i>	TGCACTGCTGAAGAACATCGG	TTGCTGTCGTTCAGAGTTGG
<i>cd68</i>	AGAAATGGAGGCCCTTGG	CTTGGCGGGTCCATAGTTGA
<i>eef1a1</i>	TGGTGGCATCGACAAGAGAAC	CCACCTTCACGCTCTGCCTTC
<i>il1-beta</i>	CATTCCCCTGGAGGGCTACA	TGACTGCCACTGAGCAGCAT
<i>il10</i>	TGCTGGATCTTAAGCACACCCTGA	TGTACAGGCCTTGTTCACGCATCT
<i>odc1</i>	GCTTCTGGAGCAGGGCAAAGGA	CCAAGCTCAGCCCCATGTCA
<i>socs3</i>	CCGGTGCTTAGGAAGAAGA	CCTTAAAGCAGCCECCATC
<i>tnf-alpha</i>	GCTCAAGGATAACTCCATCG	AACCAAGTGGCACCTGAATG

**Primers for qPCR (mice)**

Target	Forward (5'-3')	Reverse (5'-3')
<i>Ascl1</i>	TCTCCTGGGAATGGACTTTG	GGTTGGCTGTCGGTTGTT
<i>Bax</i>	AGGCCTCCTCTCCTACTTCG	CTCAGCCCCTCTTCTTCCAG
<i>Bcl2</i>	GGACTTGAAGTGCCATTGGT	AGCCCCCTCTGTGACAGCTTA
<i>Ccl2</i>	GAAGGAATGGGTCCAGACAT	ACGGGTCAACTTCACATTCA
<i>Gfap</i>	CCAGTTACCAGGAGGCACCTG	CGATGTCCAGGGCTAGCTTAA
<i>Il1-beta</i>	GCACTACAGGGCTCCGAGATGAA	TTGTCGTTGCTTGGTTCTCCTTGT
<i>Il-6</i>	GCCTTCTTGGGACTGATGCTGGT	TCCTCTGTGAAGTCTCCTCCG
<i>Rps26</i>	CCCAAGGATAAGGCCATCAAG	AAGCACGTAGGCCTGAAGA
<i>Srp72</i>	GCACTCATGGTAGCGTCCA	CACCCAGCAGACAGACAAACTG
<i>Tbp</i>	CACAGGAGCCAAGAGTGAAGAAC	ATCACAGCTCCCCACCATGT
<i>Tnf-alpha</i>	AAGTCAACCTCTCTGCC	TCCAAAGTAGACCTGCCCG

**Table S3. List of primers.**

**Supplementary Table S4.**

Sample	Condition	Raw reads	Uniquely mapped reads	Mapped length
S13	Permissive control	37519396	32584008	294.26
S11	Permissive control	55667307	48249728	294.84
S9	Permissive control	37134505	32022113	294.80
S14	Permissive <i>rho</i> crispant	55470492	48437975	294.47
S12	Permissive <i>rho</i> crispant	42054660	36682819	293.81
S10	Permissive <i>rho</i> crispant	44074067	38604360	293.86
S3	Refractory control	31671086	27404733	294.53
S5	Refractory control	38540883	33584757	294.89
S7	Refractory control	48274813	41542934	294.17
S4	Refractory <i>rho</i> crispant	49009929	42877033	294.80
S6	Refractory <i>rho</i> crispant	55657807	48465273	294.08
S8	Refractory <i>rho</i> crispant	50338069	44186472	293.79

**Table S4. RNAseq samples.**

## Supplementary Table S5.

Figure 1A							
BrdU+ cells / section				IB4+ cells / section			
Control	<i>rho</i> crispant	Control	<i>rho</i> crispant	Control	<i>rho</i> crispant	Control	<i>rho</i> crispant
0.00	1.44	0.80	4.22	1.25	4.38	5.29	46.00
0.20	1.40	1.20	3.10	1.50	4.88	6.29	134.60
0.60	0.70	1.60	2.50	1.50	7.28	5.67	75.67
0.25	0.38	0.60	3.80	1.75	8.95	6.00	51.50
0.00	0.40	2.20	6.40	2.50	9.88	6.00	160.00
0.00	1.25	1.60	5.63	2.88	10.99	5.17	114.00
0.25	1.22	0.00	6.44	3.88	23.13		
		0.00	4.33	4.63			
			5.80				
			3.40				

Figure 2A							
IB4+ cells / section				Stages			
45/46	47/48	49/50	51/52	53/54	55/56	60	66
0.125	0	0	1.83	1.33	3	11.6	13.8
0	0.166	0.5	1	3.5	2.16	10.7	9
0	0	0.5	1	1.83	3.3	9.5	10.3
0.25	0.166	0.833	1.17	1.66	3.1	7.8	6.1
0.125	0.33	1.16	1.17	1.33	1.83	9.3	
0.25	0.83	1	0.6	1.5	3	6.5	
0.125	0	0.5	0.5	2.16	2.67		

Figure 3G							
-ΔCT							
anxA1				il1-beta		il10	
Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>
-4.40	-3.03	-15.42	-13.13	-12.20	-10.94		
-6.01	-4.42	-13.56	-11.61	-11.98	-11.43		
-9.04	-4.46	-11.12	-11.33	-11.62	-10.93		
-8.56	-4.89	-11.93	-10.41	-11.14	-10.45		
-8.75	-5.22	-13.90	-12.60	-11.79	-10.67		
-4.33	-4.20	-12.32	-11.34	-13.37	-12.02		
-9.82	-4.82	-12.73	-11.36	-12.04	-10.72		
-8.99	-3.67			-11.24	-10.89		
sox3				cd68		tnf-alpha	
Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>	Control	CoCl <sub>2</sub>
-7.29	-3.93	-7.04	-3.79	-11.99	-8.69		
-7.40	-5.53	-9.10	-5.96	-11.95	-10.83		
-7.69	-5.62	-9.88	-5.88	-11.05	-9.32		
-8.48	-5.79	-9.74	-6.29	-12.08	-11.86		
-9.13	-7.30	-8.95	-6.36	-11.21	-10.39		
-8.21	-6.38	-8.58	-5.75	-13.94	-11.72		
-9.43	-5.79	-10.50	-7.05	-12.99	-11.49		
-9.34	-6.25	-8.63	-5.43				

Figure 3I		
%PCNA+ cells / Yap+ cells		
Control	CoCl <sub>2</sub>	
0	96.88	
0	89.55	
0	93.44	
0	97.89	
0	94.19	
0	96.55	
0	96.15	
0	100.00	
0	77.50	
0	83.78	

Figure 2C			
IB4+ cells / section			
Control	<i>rho</i> crispant	Control	<i>rho</i> crispant
0.56	0.00	4.18	16.20
0.00	0.00	5.55	16.40
0.00	0.10	5.50	13.08
0.00	0.00	7.50	16.91
0.00	0.90	0.58	14.83
0.25	0.00	0.27	14.58
0.00	1.00	2.27	13.92
0.00	0.54	2.83	16.50
0.45	0.38	1.67	
0.10	0.73	4.17	
0.27	0.14	8.18	
0.09	2.67	9.27	
0.00	0.91		
0.25			
0.73			
0.10			

Figure 3D			
IB4+ cells / section			
Control	CoCl <sub>2</sub>	Control	<i>rho</i> crispant
63.95	305.56	26.67	143.33
35.53	540.06	8.33	88.33
35.53	312.67	16.67	113.33
49.74	312.67	21.67	131.67
42.64	376.62	5.00	103.33
42.64	461.89	0.00	
35.53	390.83	5.00	
71.06	390.83		
92.38	341.09		
63.95	312.67		
85.27	397.94		
71.06	397.94		
49.74	476.11		
85.27	717.71		
49.74			
85.27			
42.64			
78.17			
49.74			
14.21			
28.42			
99.48			
63.95			
56.85			
63.95			
35.53			
56.85			
56.85			

Figure 3M		
PCNA+ IB4+ cells / section		
Control	CoCl <sub>2</sub>	Dex + PLX3397
3.40	285.20	134.60
4.20	266.80	119.80
10.40	330.20	22.60
0.00	300.20	20.00
1.00	287.40	97.00
1.00	244.80	132.00
0.80	91.00	190.00
6.20	150.20	120.00
0.20	341.60	38.40
1.33	331.20	125.60
	198.40	74.00
	179.00	105.40

Figure 3Q	
PCNA+ IB4+ cells / section	
<i>rho</i> crispant	Dex + PLX3397
90.60	134.00
86.20	113.60
127.80	151.60
166.20	135.00
138.40	100.20
174.40	99.40
264.80	98.60
263.40	148.20
194.00	79.80
234.20	102.40
189.00	116.60
128.20	104.80
237.00	132.60
100.60	137.20
215.20	123.00
231.40	220.00
220.80	88.00
184.60	60.40
	83.40
	101.40

Figure 4B		
IB4+ cells / section		
		CoCl <sub>2</sub>
Control	CoCl <sub>2</sub>	PLX3397
0.40	18.00	6.40
3.60	14.00	4.67
1.40	11.40	7.20
1.00	9.80	9.80
0.20	31.60	3.60
1.40	8.00	7.20
1.80	9.20	5.20
0.00	9.20	8.40
3.80		0.20
0.80		1.60
0.00		2.00
0.00		1.80
0.80		3.40

Figure 4C		
IB4+ IB4- cells / section		
		CoCl <sub>2</sub>
Control	CoCl <sub>2</sub>	PLX3397
0.40	120.50	15.40
1.00	42.60	1.33
0.00	62.00	4.00
1.50	49.20	2.80
0.60	145.40	5.60
1.40	51.80	35.40
2.60	74.20	4.80
0.00	107.60	3.60
2.80		9.20
1.80		3.60
1.00		4.40
1.60		2.60
2.00		4.00

Figure 4F	
IB4+ cells / section	
<i>rho</i> crispant	
Control	Zymosan
3.14	18.86
3.86	19.86
3.14	19.88
2.43	9.71
3.83	28.86

Figure 4G	
IB4+ IB4- cells / section	
<i>rho</i> crispant	
Control	Zymozan
7.43	11.29
4.57	10.71
3.29	16.25
5.00	6.71
4.00	11.00

Figure 4I	
IB4+ cells / section	
<i>rho</i> crispant	
Control	Bacteria
6.33	37.60
7.00	41.33
1.67	22.00
3.25	27.00
6.33	19.00
2.75	22.67
4.71	29.25
2.00	20.33
	13.50
	38.43
	25.00
	31.80
	16.29
	14.20
	29.00
	27.00
	17.00
	25.50
	25.25
	17.00
	30.67
	23.67

Figure 4J	
IB4+ IB4- cells / section	
<i>rho</i> crispant	
Control	Bacteria
7.67	8.70
2.00	3.00
1.83	11.75
3.00	6.00
13.67	16.00
2.75	6.33
4.00	3.00
3.50	6.67
	6.00
	12.14
	10.50
	9.60
	6.86
	5.00
	15.00
	16.50
	4.33
	7.50
	6.38
	4.33
	6.67
	2.33

Figure 5B												
EdU+ Sox9+ cells / field												
Control												
DEVO	0.00	0.00	0.00	0.00								
DEV1	0.00	0.00	0.00	0.00	0.00							
DEV3	7.33	2.14	3.75	0.25	0.75							
DEV5	28.63	15.38	33.00	18.13	8.63	3.00	9.00	12.75	10.25	143.67	42.86	134.71
DEV7	21.88	30.14	18.33	9.75	14.20	13.60	20.91	14.80	19.40	13.75	23.00	9.50
										108.40	163.38	180.89
										115.00	43.50	53.42
										24.22	51.20	24.22
										58.00	82.75	113.00

<b>Figure 5D</b>	
<b>CD68+ cells / field</b>	
LPS	PLX3397
56.92	9.08
51.08	12.19
62.75	11.44
44.50	10.06
39.00	13.58
69.17	14.38
68.69	12.63
30.75	

<b>Figure 5E</b>		
<b>EdU+ Sox9+ cells / field</b>		
LPS		
Control	LPS	PLX3397
24.00	79.25	36.50
28.75	149.00	16.50
28.25	59.50	2.75
32.25	61.75	25.50
37.75	108.25	55.75
62.00	77.50	47.00
60.50	182.75	47.75
33.25	65.00	36.50

<b>Figure 6A</b>	
<b>Ccl2 RNA level</b>	
Control	
DEV1	158.64 185.04 268.29 542.75 588.25 140.88 84.56 103.69
DEV3	168.39 162.01 67.45 59.85 247.73 32.16 25.91
DEV5	89.96 23.25 42.24 64.47 156.50 24.24 27.86 50.79
DEV7	37.62 13.54 32.61 100.06 12.00 72.87 29.88 25.82 62.98 8.90 10.22 16.13
LPS	
DEV1	838.51 1203.89 2224.19 334.67 2114.17 268.52 176.77 161.79
DEV3	506.16 174.68 995.67 508.97 737.61 110.42 81.31
DEV5	821.58 229.13 3380.42 357.97 122.80 198.26 122.72 108.42
DEV7	491.54 511.80 417.70 2683.91 378.85 617.54 3606.31 600.40 784.05 135.76 134.40 125.67
<b>Ilf-beta RNA level</b>	
Control	
DEV1	2.66 3.22 4.28 3.77 11.96 2.18 1.20 2.53
DEV3	1.73 1.68 0.52 3.33 1.30 0.60 0.71
DEV5	0.68 0.79 1.54 0.89 6.03 1.78 9.59 2.51 8.58 0.73 1.49 3.12
DEV7	2.60 0.76 1.99 0.89 0.87 1.96 0.82 4.13 1.72 0.81 1.16 0.69
LPS	
DEV1	22.77 32.83 41.39 7.31 33.72 4.53 4.19 4.17
DEV3	13.14 3.75 23.91 18.42 10.03 2.96 1.55 2.18
DEV5	17.50 7.41 23.63 11.62 31.68 18.84 18.54 18.26 2.45 2.39 1.97 1.30
DEV7	34.74 34.13 39.96 17.16 20.40 13.80 57.39 15.24 15.97 4.20 2.74 4.62
<b>Iif RNA level</b>	
Control	
DEV1	2.57 3.64 13.98 3.86 8.09 10.66 3.39 5.11
DEV3	4.59 2.40 3.69 3.33 2.23 0.96 0.71
DEV5	6.47 0.79 2.44 1.02 6.03 0.73 1.82 3.12
DEV7	2.60 0.76 1.99 0.81 0.85 1.95 0.76 4.13 1.73 0.82 1.16 1.07
LPS	
DEV1	19.21 38.17 45.57 13.90 24.08 34.13 17.81 19.11
DEV3	12.69 2.52 20.79 12.43 6.60 14.68 5.33 7.79
DEV5	26.65 11.65 4.89 3.56 41.74 88.59 9.64 42.32 5.79 6.08 3.00 6.71
DEV7	6.92 8.22 6.38 64.49 6.64 5.68 32.94 15.24 8.62 4.99 4.36 3.50
<b>Tnf-alpha RNA level</b>	
Control	
DEV1	3.26 4.38 2.80 9.68 4.80 0.65 0.50 1.29
DEV3	3.38 1.68 1.22 2.62 2.89 1.00 0.71
DEV5	3.27 2.63 7.35 1.82 4.75 8.06 8.96 5.79 6.68 0.73 1.49 3.15
DEV7	45.94 2.91 6.47 5.13 2.59 9.53 4.28 4.13 6.24 0.81 1.16 1.91
LPS	
DEV1	2.93 11.76 19.84 7.74 4.55 0.72 0.66 0.98
DEV3	19.70 5.53 18.36 32.23 9.38 3.13 1.64 1.72
DEV5	31.18 8.24 25.23 47.04 24.58 40.52 19.09 14.15 2.66 2.16 3.82 2.40
DEV7	55.47 16.48 16.78 20.43 32.14 13.62 12.02 15.24 16.14 5.62 4.54 4.34

<b>Figure 6C</b>				
<b>EdU+ Sox9+ cells / field</b>				
TNF-alpha				
Control	LPS	TNF-alpha	IL6	+ IL-6
8.00	59.67	255.71	7.25	116.50
6.33	101.20	257.63	9.00	132.50
3.43	134.57	157.13	4.33	156.25
27.00	64.25	117.67	4.33	152.29
36.13	93.25	77.29	9.71	117.13
6.63	56.00	138.63	34.88	
8.63		113.13	31.38	
		73.50	17.17	
			15.50	

<b>Figure 6E</b>		
<b>Tnf-alpha mRNA level</b>		
LPS		
Control	LPS	PLX3397
2.46	2.82	1.06
0.40	5.61	5.58
1.32	8.22	2.54
0.78	4.42	1.07
0.75	2.90	1.23
1.34	1.85	1.18
0.81	1.68	1.80
1.23	1.53	1.58

<b>Figure 7B</b>	
<b>EdU+ Sox9+ cells / field</b>	
Control AAV	
Control AAV	
AAV-YAP5SA	
AAV-YAP5SA	
LPS	
57.63	73.00
33.13	83.75
37.38	106.71
48.25	105.75
63.50	112.63
	308.00
	264.75
101.25	

<b>Figure 7D</b>			
EdU+ Sox9+ cells / field			
Control	LPS	EGF	EGF LPS
0.38	124.38	331.63	623.25
22.75	132.88	20.50	877.13
7.13	183.38	559.00	672.29
5.00	237.38	351.63	308.83
13.71	308.38	67.71	450.38
8.14	59.25	167.33	310.28
2.00	489.75	90.43	239.88
6.60	116.83	49.00	135.33
9.25	24.67	290.20	312.43
53.38	91.75	639.25	432.88
12.00	172.25	231.00	115.00
10.88	46.50	69.88	408.63
54.63	130.63	27.50	295.00
39.00	23.25	158.63	67.38
	46.88	22.75	217.63
	77.00	410.88	253.00
	156.88		364.25
	85.50		

<b>Figure 7F</b>			
EdU+ Sox9+ cells / field			
	Control AAV PLX3397	AAV-YAP5SA PLX3397	AAV-YAP5SA PLX3397
	12.50	1.57	962.14
	30.75	0.88	729.00
	9.56	1.14	924.17
	12.75	2.00	824.13
	11.43	1.88	880.00
		1.75	135.63
		2.14	131.25
		0.67	137.25
		3.00	206.00
			273.50
			282.29

<b>Figure 7H</b>			
EdU+ Sox9+ cells / field			
Control	PLX3397	EGF	EGF PLX3397
4.88	0.71	186.80	10.25
3.40	0.13	51.75	8.17
2.20	0.50	49.33	15.67
26.43	0.83	55.33	9.83
43.17	3.86	75.50	71.50
14.80	2.57	181.29	62.75
57.00	4.00	178.75	10.60
		173.60	

<b>Figure 8A</b>	
Ascl1 mRNA level	
Control	LPS
0.74	0.99
0.90	1.22
0.80	1.10
2.42	1.42
0.64	0.90
0.95	0.41
1.62	0.63
0.78	0.41
0.97	0.39
1.38	0.74
0.75	0.52
1.00	0.40
0.53	1.94
1.40	0.39
1.35	0.47
2.72	0.78
0.53	1.85
0.84	0.65
0.84	0.80
1.20	0.56
0.84	0.98
0.93	0.59
1.08	2.18
1.38	1.17
0.67	0.82
0.83	0.87
1.37	0.73
1.65	1.00
0.69	0.63
0.74	0.79
1.17	1.17
1.10	1.16
0.95	0.65
1.01	0.96
0.83	0.77
1.11	0.91
1.07	0.65
	0.12

<b>Figure 8D</b>			
<b>Ascl1 mRNA level</b>			
LPS			
Control	PLX3397	LPS	PLX3397
1.18	2.13	5.24	6.10
0.85	1.19	6.04	7.39
0.58	1.42	2.85	9.22
0.42	1.48	1.25	5.06
1.90	2.30	1.29	5.43
0.69	1.15	1.90	4.25
2.09	1.92	3.75	5.12
1.51		1.48	2.80
1.27		2.97	5.44
0.69		1.94	9.29
0.94		1.22	2.37
1.63		1.67	4.28
0.76		1.62	2.93
0.98		1.29	5.13
		0.98	5.01
			2.90

<b>Figure 9A</b>			
<b>Tnf-alpha mRNA level</b>			
LPS			
Control	LPS	PLX3397	
1.07	5.23	2.39	
0.68	2.97	1.56	
0.88	6.12	5.20	
1.02	4.32	2.38	
1.16	6.04	0.79	
1.33	2.40	0.96	
1.33	2.26	0.81	
0.67	6.88	1.38	
1.46	0.65	0.95	
1.63	1.23	0.70	
0.62	2.73	0.25	
0.75		0.65	
0.98		0.76	
0.63		1.39	
1.95		2.45	
1.12		0.42	

<b>Figure 9B</b>		
<b>Ascl1 mRNA level</b>		
LPS		
Control	LPS	TNF-alpha
0.78	0.72	0.59
1.39	0.46	0.44
1.05	0.60	0.52
1.07	0.74	0.50
0.82	0.78	0.45
1.10	1.29	0.57
1.12	0.40	0.37
1.05	1.03	0.53
0.78	0.27	0.21
0.99	0.59	0.31
	0.45	0.52
		0.50

<b>Figure 9C</b>			
<b>Ascl1 mRNA level</b>			
TNF-alpha			
TNF-alpha	PLX3397		
1.79	2.52		
1.16	4.53		
1.23	2.80		
0.73	2.50		
1.06	3.26		
	6.65		

<b>Figure 9D</b>			
<b>Ascl1 mRNA level</b>			
LPS			
Control	LPS	PLX3397	TNF-alpha
0.93	5.59	0.22	
1.46	1.95	0.23	
0.71	4.18	0.14	
	4.30	0.50	
	2.67	0.21	
		0.41	
		0.45	
		0.54	

<b>Figure S1</b>			
<b>BrdU+ cells / section normalized to the retina surface (a.u.)</b>			
rho crispant			
Control	rho crispant	Control	rho crispant
0.00	0.13	0.07	0.74
0.02	0.12	0.09	2.30
0.05	0.06	0.07	1.60
0.02	0.03	0.09	0.84
0.00	0.04	0.09	3.40
0.00	0.11	0.08	2.00
0.02	0.12		

<b>Figure S5B</b>	
IB4+ cells / section	
CoCl <sub>2</sub>	
CoCl <sub>2</sub>	Dex + PLX3397
24.40	9.60
55.60	14.60
27.00	4.20
34.60	4.00
15.00	9.00
20.00	10.60
18.00	11.40
	9.20
	4.00
	6.80
	1.60
	16.20
	7.00
	16.20
	12.00
	2.60
	2.80
	3.80
	7.00

<b>Figure S5D</b>	
IB4+ cells / section	
rho crispant	
rho crispant	Dex + PLX3397
19.60	6.60
19.40	4.40
24.60	5.80
5.40	8.40
11.00	3.80
21.60	11.60
15.00	10.60
7.40	11.20
21.80	6.80
18.20	6.40
11.40	6.00
22.60	6.40
9.00	9.80
15.20	13.40
12.00	9.00
15.20	15.20
10.60	11.75
18.60	10.20
	11.60
	6.00

<b>Figure S7B</b>														
Bax/Bcl2 mRNA level														
	Control							LPS						
DEV0	0.78	1.28	0.75	1.03	0.92	1.42	0.87	1.17	0.95	1.01				
DEV1	4.41	4.65	2.94	4.22	3.85	3.08	2.18				4.80	3.42	4.68	
DEV3	2.95	4.70	4.91	6.14	2.45	2.87					5.05	3.67	3.17	
DEV5	4.07	4.64	8.22	5.20	2.46	2.15	2.31				5.10	5.96	4.23	
DEV7	4.35	5.01	6.04	2.80	3.73	5.44	2.42	4.54	3.61	3.91	2.98	4.27	4.12	2.96

<b>Figure S7C</b>													
Gfap mRNA level													
	Control							LPS					
DEV0	1.41	0.77	1.83	0.51	0.49	0.47	1.67	2.63					
DEV1	4.14	1.98	1.85	5.34	2.65						1.93	3.92	2.46
DEV3	37.99	48.97	24.37	25.55	44.27						12.60	17.26	41.88
DEV5	15.34	12.70	35.27	18.54	79.47	72.95	101.04	50.19	106.42		56.53	29.31	56.22
DEV7	64.08	22.55	55.45	165.57	189.83	364.64	284.90	81.62	56.09		25.83	27.19	24.76

<b>Figure S8B</b>		
Sox9+ cells / field		
LPS		
Control	LPS	PLX3397
363	365	307
324	374	303
255	366	416
457	318	488
434	353	337
461	382	454
371	439	350
400	423	

<b>Figure S8C</b>			
Bax/Bcl2 mRNA level			
LPS			
Control	LPS	PLX3397	PLX3397
0.77	1.09	1.16	1.18
1.25	0.72	1.02	1.30
0.80	0.97	1.17	1.06
1.18	0.89	0.91	0.84
		1.18	0.94

<b>Figure S9B</b>			
CD68+ cells / field			
LPS			
LPS	PLX5622	PLX5622	PLX5622
34.13	8.00		
33.88	10.13		
39.38	8.50		
43.14	2.75		
46.75	8.38		
	6.88		

<b>Figure S9C</b>			
EdU+Sox9+ cells / field			
LPS			
LPS	PLX5622	PLX5622	PLX5622
81.25	55.25		
86.38	36.00		
81.13	70.25		
44.63	18.88		
120.38	24.38		
	22.63		

**Table S5. Descriptive Statistics.**