

Figure S1: Significant changes in refractive error (Diopter) observed in *Adipor1*^{-/-} and *Mfrp*^{rd6} mice, by 10 weeks of age, **** p > 0.0001.

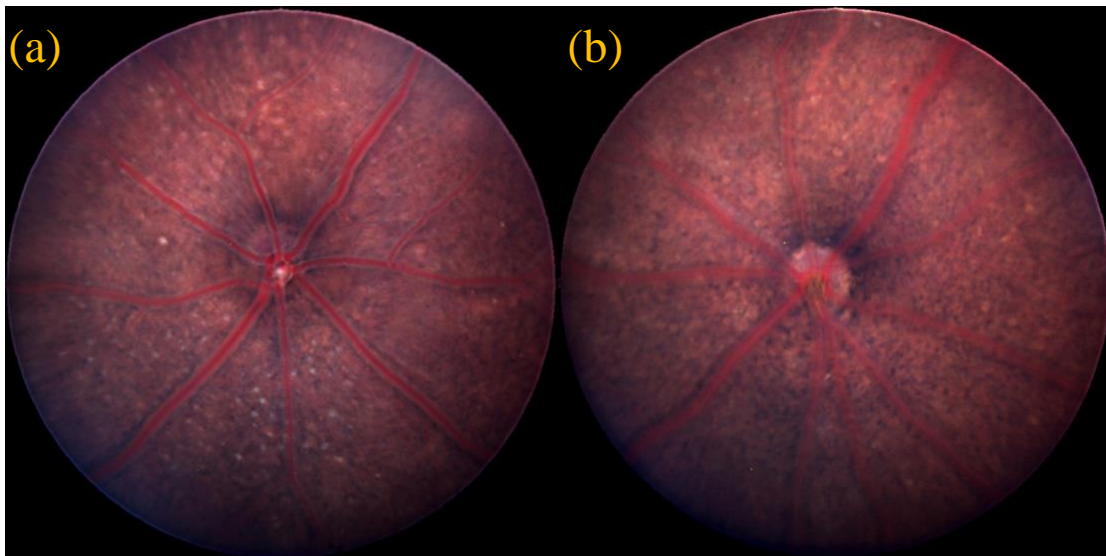


Figure S2: Spots observed by fundus photodocumentation in 10-week-old (a) double heterozygous (*Adipor1*^{+/-}/*Mfrp*^{+/-rd6}) and (b) single heterozygous *Adipor1*^{+/-} mice. N= 5.

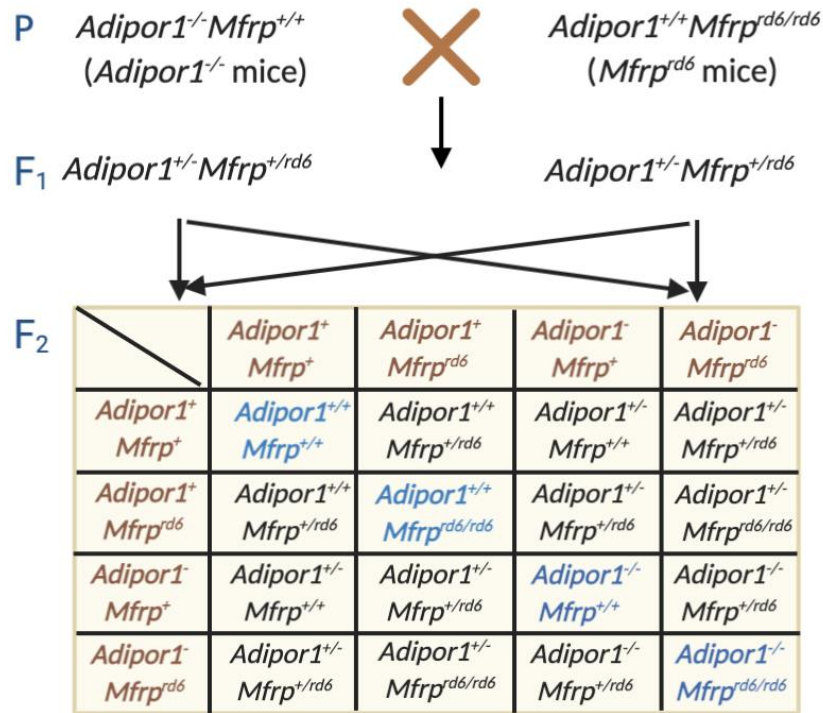


Figure S3: Generation of (*Adipor1*^{tm1Dgen} × *Mfrp*^{rd6}) F2 intercross progeny. Single gene *Adipor1*^{-/-} and *Mfrp*^{rd6} mutant mice were crossed to produce *Adipor1*/*Mfrp* double heterozygous mice (F1). The double heterozygous mice were intercrossed to produce F2 mice with nine possible genotypic combinations as shown in the 16 Punnett square.

Source	Nparm	DF	Sum of Squares	F Ratio	Prob>F
Adipor1	2	2	1.7333333	18.5589	<.0001
Mfrp	2	2	2.6027778	27.8681	<.0001
Adipor1*Mfrp	4	4	1.8930577	10.1346	<.0001

Table S1: Effect tests obtained from fit model analysis of fundal spots, with the Prob>F = <0.0001 for both individual gene and gene interaction effects, confirming significant effect due to individual mutations as well as due to gene interaction.

Term	Estimate	Std Error	T Ratio	Prob> t
Intercept	0.2	0.096642	2.07	0.0434
Adipor1[1-0]	0.6	0.136672	4.39	<.0001
Adipor1[2-1]	0.2	0.136672	1.46	0.1493
Mfrp[1-0]	-0.075	0.123195	-0.61	0.5453
Mfrp[2-1]	0.875	0.123195	7.10	<.0001
Adipor1[1-0]*Mfrp[1-0]	0.275	0.17084	1.61	0.1134
Adipor1[1-0]*Mfrp[2-0]	-0.875	0.166222	-5.26	<.0001
Adipor1[2-1]*Mfrp[1-0]	-0.2	0.166222	-1.18	0.2417
Adipor1[2-1]*Mfrp[2-1]	-1.37e-15	0.151097	-0.00	1.0000

Table S2: Parameter estimates (the change in the response associated with a one-unit change of the predictor, all other predictors being held constant) obtained from fit test analysis for fundal spots, showing which variables/predictor have significant influence on the response. The genotypes were considered ordinal variables with 0 – Wild type; 1- heterozygous and 2- homozygous.

Source	Nparm	DF	Sum of Squares	F Ratio	Prob>F
Adipor1	2	2	15.308814	216.9900	0.0074
Mfrp	2	2	14.799119	209.7655	<.0001
Adipor1*Mfrp	4	4	5.946472	42.1432	0.5715

Table S3: Effect tests obtained from fit model analysis for axial length, with the Prob>F = <0.05 for both the individual gene contributions. Gene interaction effect is non-significant, confirming the absence of interaction between *Adipor1* and *Mfrp* for determining axial length.

Term	Estimate	Std Error	T Ratio	Prob> t
Intercept	3.2392857	0.012345	262.40	<.0001
Adipor1[1-0]	-0.00458	0.01667	-0.27	0.7839
Adipor1[2-1]	-0.055956	0.019804	-2.83	0.0053
Mfrp[1-0]	-0.005649	0.015791	-0.36	0.7210
Mfrp[2-1]	-0.107922	0.014092	-7.66	<.0001
Adipor1[1-0]*Mfrp[1-0]	-0.000857	0.020434	-0.04	0.9666
Adipor1[1-0]*Mfrp[2-0]	0.0177221	0.018653	0.95	0.3434
Adipor1[2-1]*Mfrp[1-0]	0.0110892	0.024023	0.46	0.6449
Adipor1[2-1]*Mfrp[2-1]	0.0111524	0.021071	0.53	0.5973

Table S4: Parameter estimates (the change in the response associated with a one-unit change of the predictor, all other predictors being held constant) obtained from fit test analysis for axial length, showing which variables/predictor have significant influence on the response. The genotypes were considered ordinal variables with 0 – Wild type; 1- heterozygous and 2- homozygous.

Source	Nparm	DF	Sum of Squares	F Ratio	Prob>F
<i>Adipor1</i>	2	2	15.308814	216.9900	<.0001
<i>Mfrp</i>	2	2	14.799119	209.7655	<.0001
<i>Adipor1*Mfrp</i>	4	4	5.946472	42.1432	<.0001

Table S5: Effect Tests obtained from fit model analysis for PR degeneration, with the Prob>F = <0.0001 for both individual gene and gene interaction effects, confirming significant effect due to individual mutations as well as due to gene interaction.

Term	Estimate	Std Error	T Ratio	Prob> t
Intercept	2.5097667	0.062606	40.09	<.0001
Adipor1[1-0]	-0.239121	0.081443	-2.94	0.0041
Adipor1[2-1]	-1.434896	0.081443	-17.62	<.0001
Mfrp[1-0]	0.0041458	0.08282	0.05	0.9602
Mfrp[2-1]	-1.278356	0.071724	-17.82	<.0001
Adipor1[1-0]*Mfrp[1-0]	-0.20185	0.110843	-1.82	0.0714
Adipor1[1-0]*Mfrp[2-0]	0.1241006	0.101042	1.23	0.2221
Adipor1[2-1]*Mfrp[1-0]	0.1884038	0.108932	1.73	0.0866
Adipor1[2-1]*Mfrp[2-1]	0.9040249	0.101481	8.91	<.0001

Table S6: Parameter Estimates (the change in the response associated with a one-unit change of the predictor, all other predictors being held constant) obtained from fit test analysis for PR degeneration, showing which variables/predictor have significant influence on the response. The near-zero coefficients indicate the variables with very little influence on the response. The variables with Prob>|t|= <0.05 are considered to have significant influence on response (PR degeneration in this case). The genotypes were considered ordinal variables with 0 – Wild type; 1- heterozygous and 2- homozygous.

Adipor1	Mfrp	Spots
0	0	0
0	0	0
0	0	0
0	0	1
0	0	0
0	1	0
0	1	0
0	1	1
0	1	0
0	1	0
0	1	0
0	1	0
0	1	0
1	0	1
1	0	0
1	0	1
1	0	1
1	0	1
1	1	1
1	1	1
1	1	1

[illegible]

2	2	1
2	2	1

Supplementary Table S7: Data from fundus spot analysis: Nine genotypic combinations of *Adipor1/Mfrp* double mutants used as independent variables, and data from fundus spot used as a response variable for factorial ANOVA. The genotypes were given variables with 0 – Wild type; 1- heterozygous and 2- homozygous.

Adipor1	Mfrp	Axial length
0	0	3.27
0	0	3.27
0	0	3.18
0	0	3.26
0	0	3.25
0	0	3.27
0	0	3.24
0	0	3.2
0	0	3.2
0	0	3.25
0	0	3.27
0	0	3.23
0	0	3.23
0	0	3.23
0	1	3.27
0	1	3.22
0	1	3.14
0	1	3.15
0	1	3.2
0	1	3.27
0	1	3.25
0	1	3.26
0	1	3.23
0	1	3.29
0	1	3.32
0	1	3.28
0	1	3.26
0	1	3.24
0	1	3.26

0	1	3.29
0	1	3.24
0	1	3.2
0	1	3.17
0	1	3.13
0	1	3.25
0	1	3.22
1	0	3.15
1	0	3.27
1	0	3.29
1	0	3.27
1	0	3.23
1	0	3.26
1	0	3.24
1	0	3.3
1	0	3.29
1	0	3.28
1	0	3.21
1	0	3.19
1	0	3.29
1	0	3.14
1	0	3.22
1	0	3.17
1	0	3.19
1	1	3.23
1	1	3.24
1	1	3.25
1	1	3.2
1	1	3.3
1	1	3.19
1	1	3.25
1	1	3.15
1	1	3.27
1	1	3.15
1	1	3.14
1	1	3.24
1	1	3.21
1	1	3.13
1	1	3.26

1	1	3.25
1	1	3.24
1	1	3.2
1	1	3.27
1	1	3.25
1	1	3.22
1	1	3.32
1	1	3.25
1	1	3.32
1	1	3.26
1	1	3.2
1	1	3.26
1	1	3.28
1	1	3.2
1	1	3.26
1	1	3.24
1	1	3.14
1	1	3.25
1	1	3.24
1	1	3.3
1	1	3.23
1	1	3.27
1	1	3.28
1	1	3.17
1	1	3.29
1	1	3.24
1	1	3.15
1	1	3.23
1	1	3.14
1	1	3.16
1	1	3.22
1	1	3.29
1	1	3.24
1	1	3.19
1	1	3.15
0	2	3.1
0	2	3.1
0	2	3.11
0	2	3.15

0	2	3.07
0	2	3.07
0	2	3.08
0	2	3.05
0	2	3.19
0	2	3.18
0	2	3.16
0	2	3.17
0	2	3.15
0	2	3.18
0	2	3.08
0	2	3.14
0	2	3.13
0	2	3.16
0	2	3.14
0	2	3.13
0	2	3.1
1	2	3.18
1	2	3.13
1	2	3.12
1	2	3.14
1	2	3.1
1	2	3.12
1	2	3.17
1	2	3.11
1	2	3.18
1	2	3.17
1	2	3.19
1	2	3.14
1	2	3.19
1	2	3.06
1	2	3.1
1	2	3.18
1	2	3.09
1	2	3.13
1	2	3.14
1	2	3.12
2	0	3.14
2	0	3.11

2	0	3.17
2	0	3.19
2	0	3.24
2	0	3.13
2	0	3.2
2	0	3.25
2	1	3.14
2	1	3.18
2	1	3.19
2	1	3.22
2	1	3.21
2	1	3.2
2	1	3.18
2	1	3.14
2	1	3.24
2	1	3.11
2	1	3.16
2	1	3.19
2	1	3.23
2	1	3.22
2	1	3.14
2	2	3.06
2	2	3.16
2	2	3.07
2	2	3.04
2	2	3.02
2	2	3.09
2	2	3.11
2	2	3.07
2	2	3.12
2	2	3.11
2	2	3.18
2	2	3.19
2	2	3.11
2	2	3.13

Supplementary Table S8: Data for axial length measurement: Nine genotypic combinations of *Adipor1/Mfrp* double mutants used as independent variables, and axial length values used as response variable for factorial ANOVA. The genotypes were given variables with 0 – Wild type; 1- heterozygous and 2- homozygous.

Adipor1	Mfrp	Degeneration
0	0	2.42275
0	0	2.0892
0	0	2.13795
0	0	2.5481
0	0	2.9754
0	0	2.28405
0	0	2.72015
0	0	2.6268
0	0	2.7835
1	0	2.0561
1	0	2.22615
1	0	1.8972
1	0	1.91605
1	0	2.37375
1	0	2.08895
1	0	2.64365
1	0	2.20335
1	0	2.49975
1	0	2.40045
1	0	2.60085
1	0	2.31475
1	0	2.2974
0	1	2.69445
0	1	2.609
0	1	2.6468
0	1	2.405
0	1	2.4836
0	1	2.78175
0	1	2.5266
0	1	2.7052
0	1	2.3637
0	1	2.4565
0	1	2.2522
0	1	2.24215
1	1	1.7352
1	1	2.04475
1	1	1.602
1	1	2.1799

1	1	2.25375
1	1	2.10175
1	1	2.39535
1	1	2.3806
1	1	2.3753
1	1	1.8931
1	1	2.21065
1	1	1.73435
1	1	2.04155
2	1	1.0181
2	1	0.8398
2	1	0.6133
2	1	0.8096
2	1	0.8088
2	1	1.11765
2	1	0.8202
2	1	0.79155
2	1	0.842
2	1	0.8644
2	1	0.6809
2	1	0.8162
2	1	0.78275
2	1	0.76505
2	0	0.7912
2	0	0.8514
2	0	0.6231
2	0	0.83225
2	0	0.7795
2	0	1.06085
2	0	0.7645
2	0	0.99525
2	0	0.8237
0	2	1.69335
0	2	0.92985
0	2	1.2851
0	2	1.2436
0	2	1.5099
0	2	1.22505
0	2	1.2739

0	2	1.4026
0	2	1.2816
0	2	1.25285
0	2	1.21845
0	2	1.1887
0	2	1.1814
0	2	0.86005
0	2	1.09275
0	2	1.12975
1	2	0.9421
1	2	0.98605
1	2	0.83615
1	2	1.12595
1	2	1.1025
1	2	0.8048
1	2	0.9176
1	2	0.8773
1	2	0.9759
1	2	0.8569
1	2	0.9467
1	2	0.85795
1	2	0.92605
1	2	0.8136
1	2	0.81075
2	2	0.5882
2	2	0.5703
2	2	0.5695
2	2	0.5357
2	2	0.6014
2	2	0.66885
2	2	0.571
2	2	0.5088
2	2	0.5111
2	2	0.68265
2	2	0.4601
2	2	0.5615
2	2	0.66175

Supplementary Table S9: Data for PR degeneration: Nine genotypic combinations of *Adipor1/Mfrp* double mutants used as independent variables, and PR nuclear count values used as response variable for factorial ANOVA. The genotypes were given variables with 0 – Wild type; 1- heterozygous and 2- homozygous.