Supplementary figures:

Next generation sequencing identifies novel disease-associated BEST1 mutations in Bestrophinopathy patients

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Short title: Mutations in Best disease
Key Words: Retina, Bestrophin, Vitelliform macular degeneration, exome sequencing.

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Supplementary Figure Legends:

Supplementary Figure S1: FAMILY A. Sibling (II.2, a) OCT of the sibling showing cystoid (white Asterix) and schitic changes in inner and outer nuclear layers of retina. ERG of the proband (b, c) and sibling (II.2, d, e) showing rod cone dysfunction. EOG of the proband (f, g) and sibling (II.2, h, i) showing minimal light rise and no light rise, respectively.

Supplementary Figure S2: FAMILY B. (a, b) ERG showing rod cone dysfunction in proband. EOG (c, d) showed an absence of light peak in the proband.

Supplementary Figure S3: Family C. (a-c) OCT showing hyper reflective RPE cell Layer(Black Arrow) with a serous subretinal fluid (White Asterix) with focal schitic changes (White Arrow) in proband's affected brother (II.1, a), brother (II.4, b) and sister (II.2, c). (d-g) Proband's (II.3) ERG (d,e) was normal and EOG (f, g) showed absence of light rise.

Supplementary Figure S4: Family D. (a-b) OCT showing focal subretinal fluid (White Arrow) in the left eye of the proband's father (I.1, a) in family D. Sibling (II.2, b) OCT was normal. (c-f) Proband (II.1) ERG (c, d) and EOG (e, f) was abnormal.

Supplementary Figure S5: Exome sequencing depth and coverage across samples sequenced in the study.

Supplementary Figure S6: Kinship coefficients between the sequenced family members confirmed their relationship.

Supplementary Figure S7: Representative Sanger sequence chromatograms of members in family A showing BEST1 p.Tyr131Cys mutation.

Supplementary Figure S8: Representative Sanger sequence chromatograms of members in family B showing BEST1 p.Arg150Pro mutation.

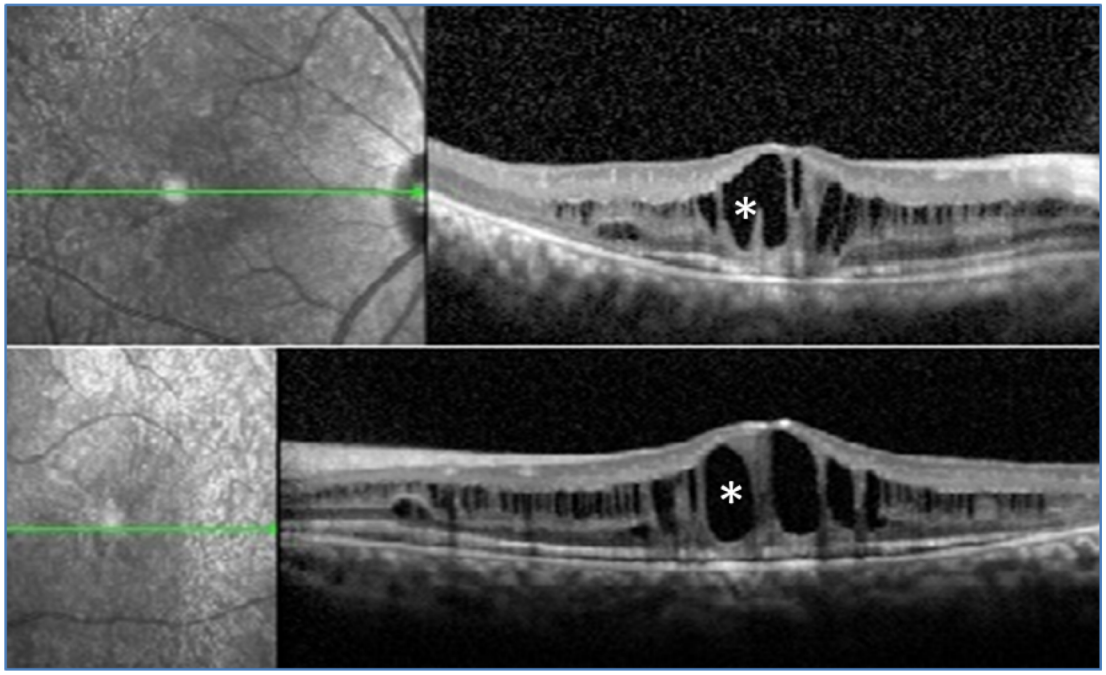
Supplementary Figure S9: Representative Sanger sequence chromatograms of members in family C showing BEST1 p.Arg47His mutation.

Supplementary Figure S10: IGV visualization of reads spanning BEST1 p.Val216Ile mutation in members of family C.

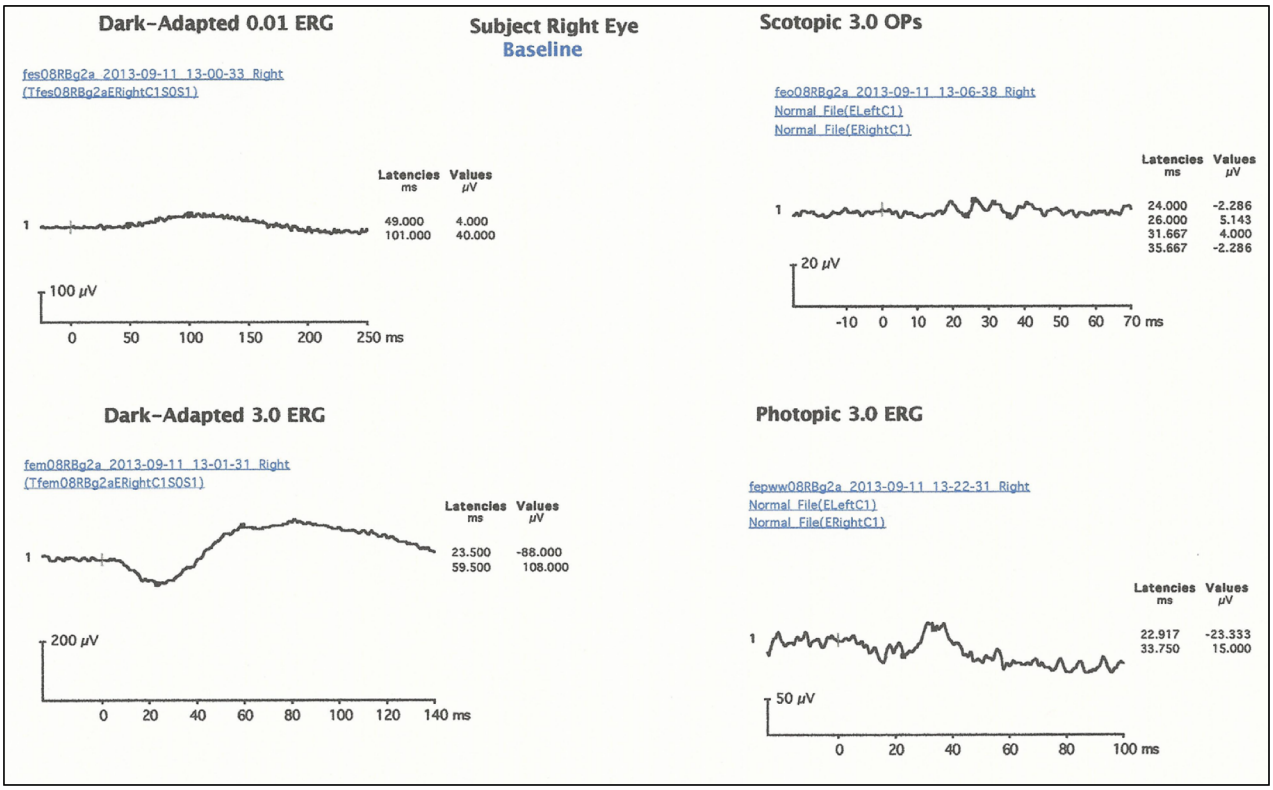
Supplementary Figure S11: Representative Sanger sequence chromatograms of members in family D showing BEST1 p.Thr91Ile mutation.

Supplementary Figure S1

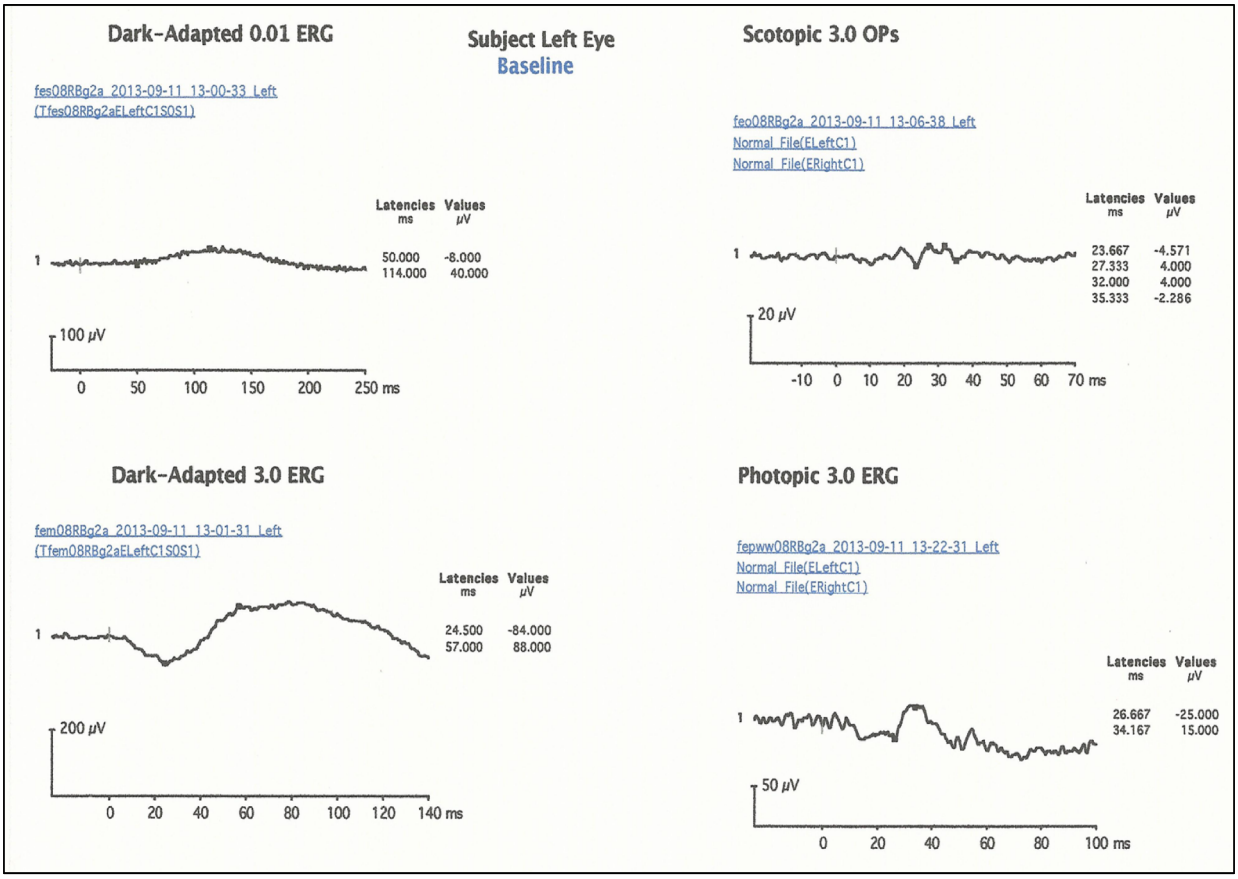
S1a



S1b



S1c


Dark-Adapted 0.01 ERG
Subject Left Eye
Baseline
fes08RBg2a 2013-09-11 13-00-33 Left
(Tfes08RBg2aELeftC1S0S1)
Latencies ms
Values µV
50.000 -8.000
114.000 40.000
100 µV
0 50 100 150 200 250 ms
Scotopic 3.0 OPs
feo08RBg2a 2013-09-11 13-06-38 Left
Normal File(ELeftC1)
Normal File(ERightC1)
Latencies ms
Values µV
23.667 -4.571
27.333 4.000
32.000 4.000
35.333 -2.286
20 µV
-10 0 10 20 30 40 50 60 70 ms
Dark-Adapted 3.0 ERG
fem08RBg2a 2013-09-11 13-01-31 Left
(Tfem08RBg2aELeftC1S0S1)
Latencies ms
Values µV
24.500 -84.000
57.000 88.000
200 µV
0 20 40 60 80 100 120 140 ms
Photopic 3.0 ERG
fepww08RBg2a 2013-09-11 13-22-31 Left
Normal File(ELeftC1)
Normal File(ERightC1)
Latencies ms
Values µV
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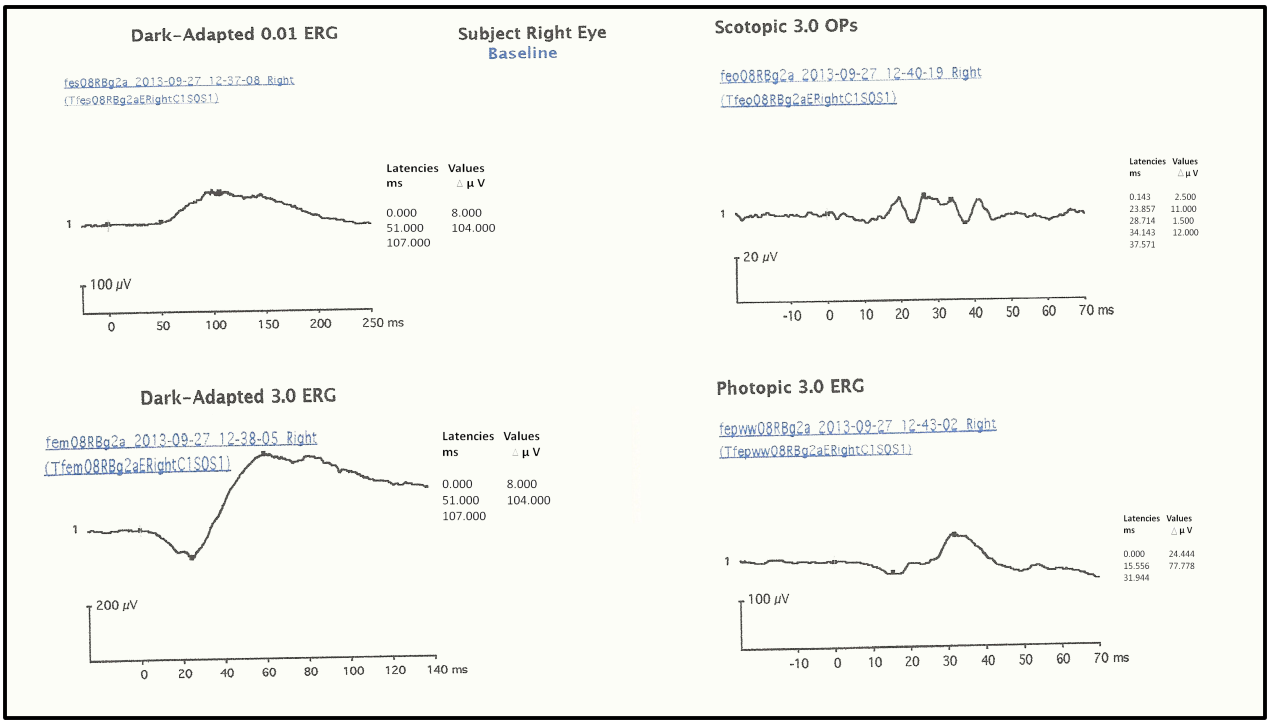
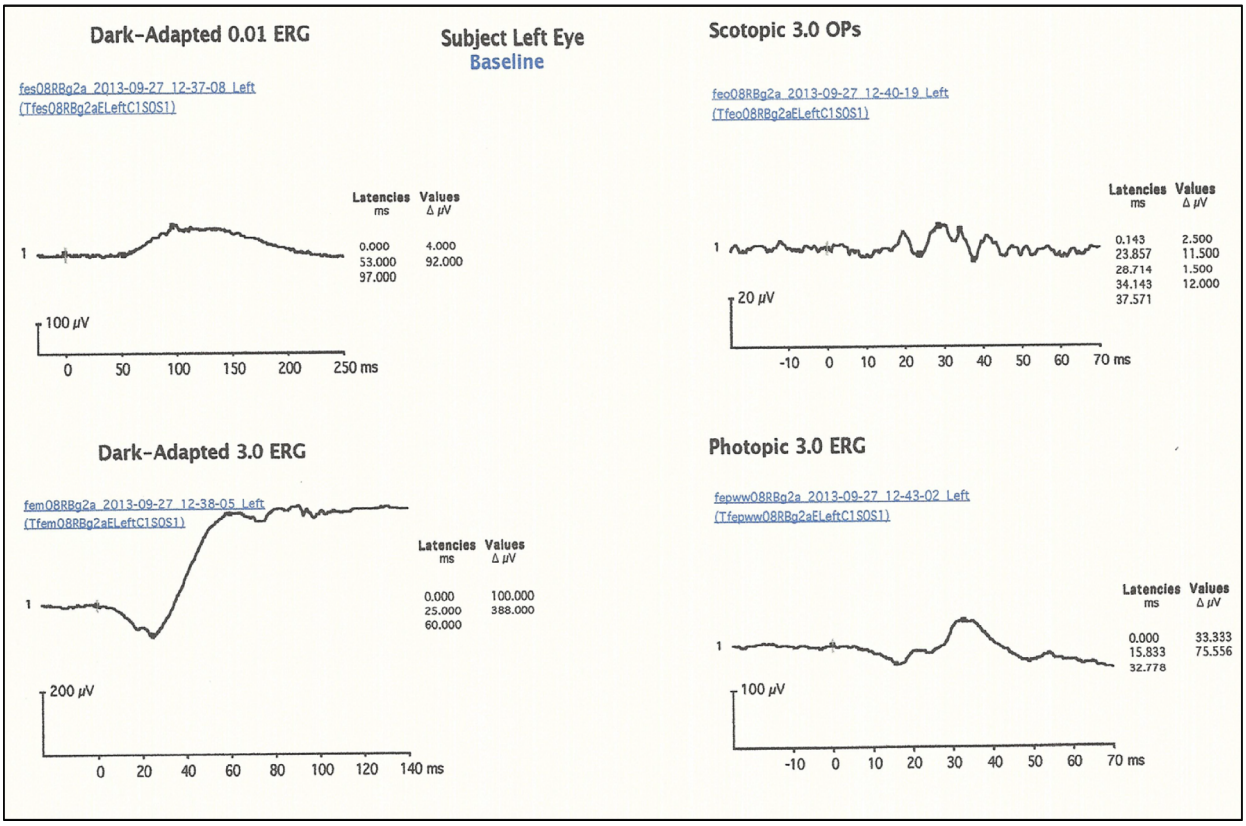
34.167 15.000
50 µV
0 20 40 60 80 100 ms

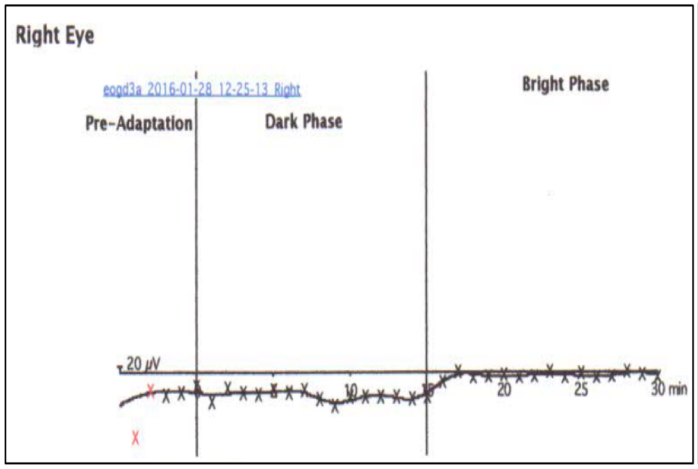
S1d


Dark-Adapted 0.01 ERG
Subject Right Eye
Baseline
fes08RBg2a 2013-09-27 12-37-08 Right
(Tfes08RBg2aERightC1S0S1)
Latencies ms
Values µV
0.000 8.000
51.000 104.000
107.000
100 µV
0 50 100 150 200 250 ms
Scotopic 3.0 OPs
feo08RBg2a 2013-09-27 12-40-19 Right
(Tfeo08RBg2aERightC1S0S1)
Latencies ms
Values µV
0.143 2.500
23.857 11.000
28.714 1.500
34.143 12.000
37.571
20 µV
-10 0 10 20 30 40 50 60 70 ms
Dark-Adapted 3.0 ERG
fem08RBg2a 2013-09-27 12-38-05 Right
(Tfem08RBg2aERightC1S0S1)
Latencies ms
Values µV
0.000 8.000
51.000 104.000
107.000
200 µV
0 20 40 60 80 100 120 140 ms
Photopic 3.0 ERG
fepww08RBg2a 2013-09-27 12-43-02 Right
(TfepwwO8RBg2aERightC1S0S1)
Latencies ms
Values µV
0.000 24.444
15.556 77.778
31.944
100 µV
-10 0 10 20 30 40 50 60 70 ms

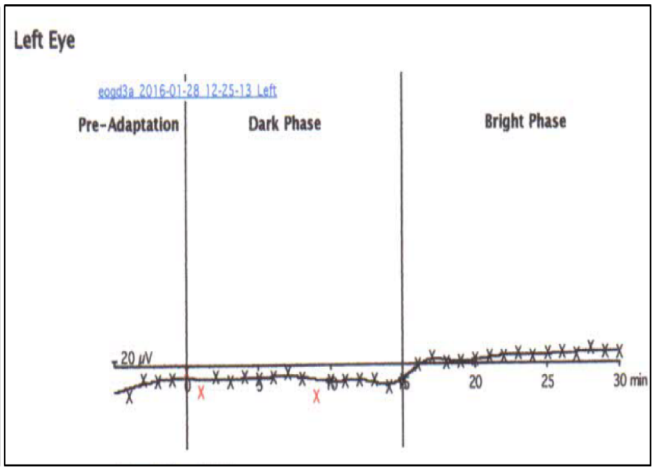
S1e



S1f



S1g



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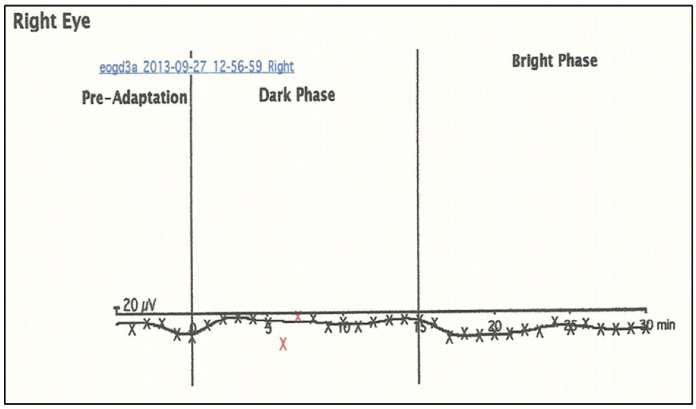
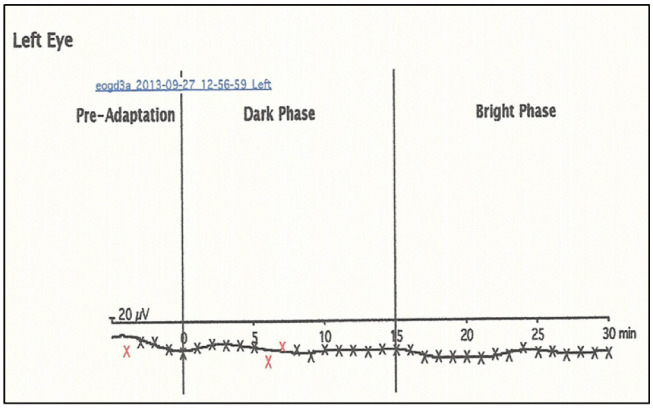
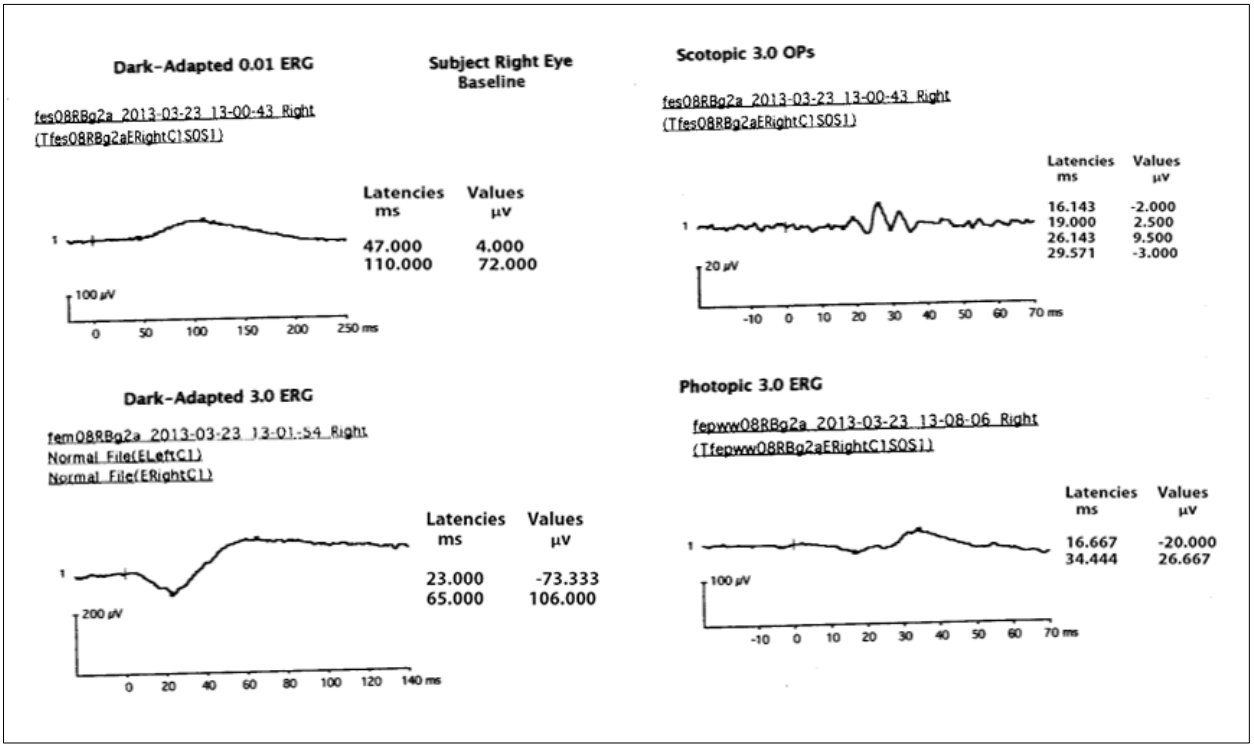


S1i

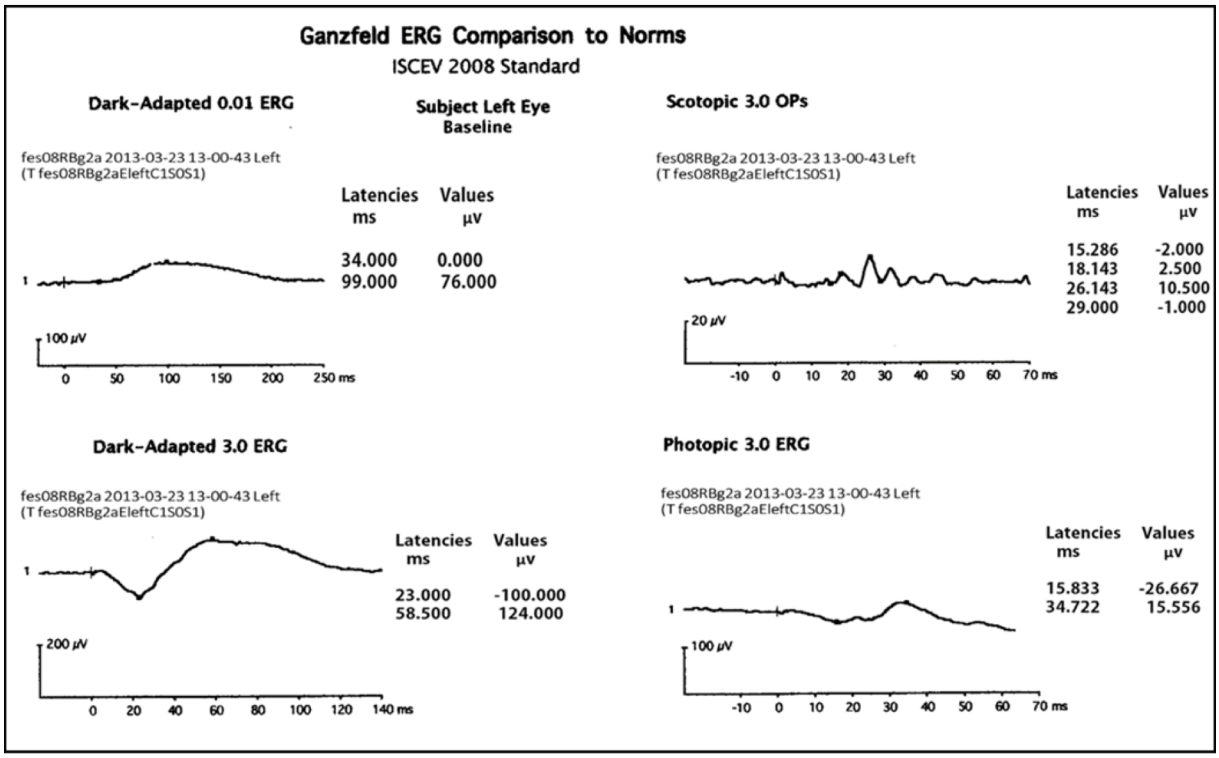


Supplementary Figure S2

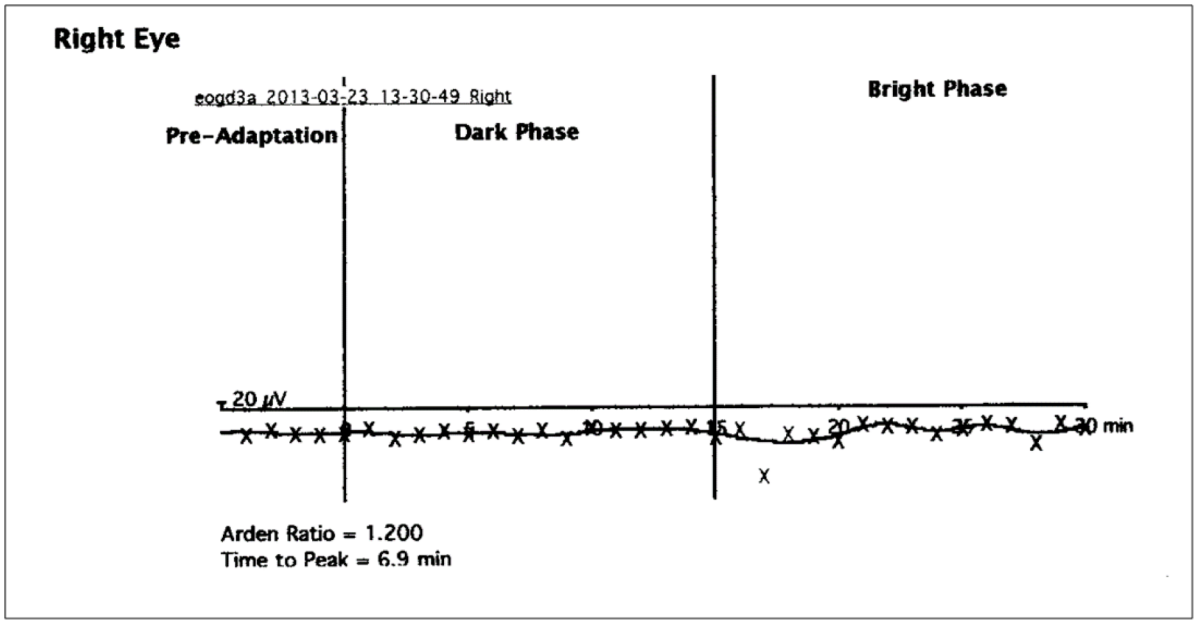
S2a



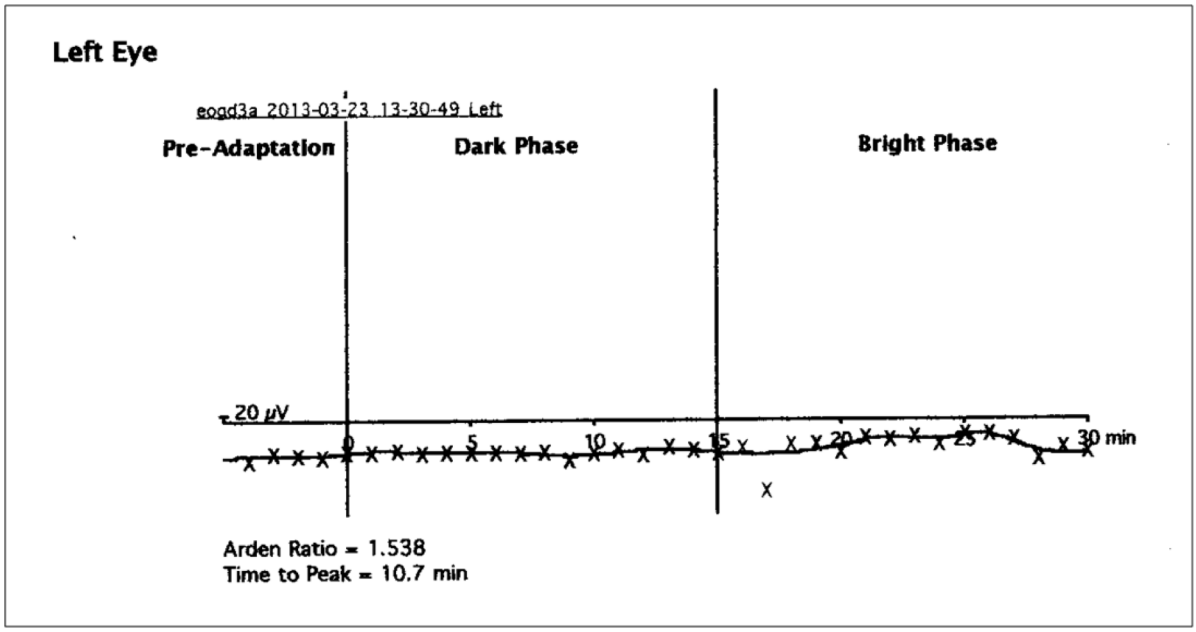
S2b



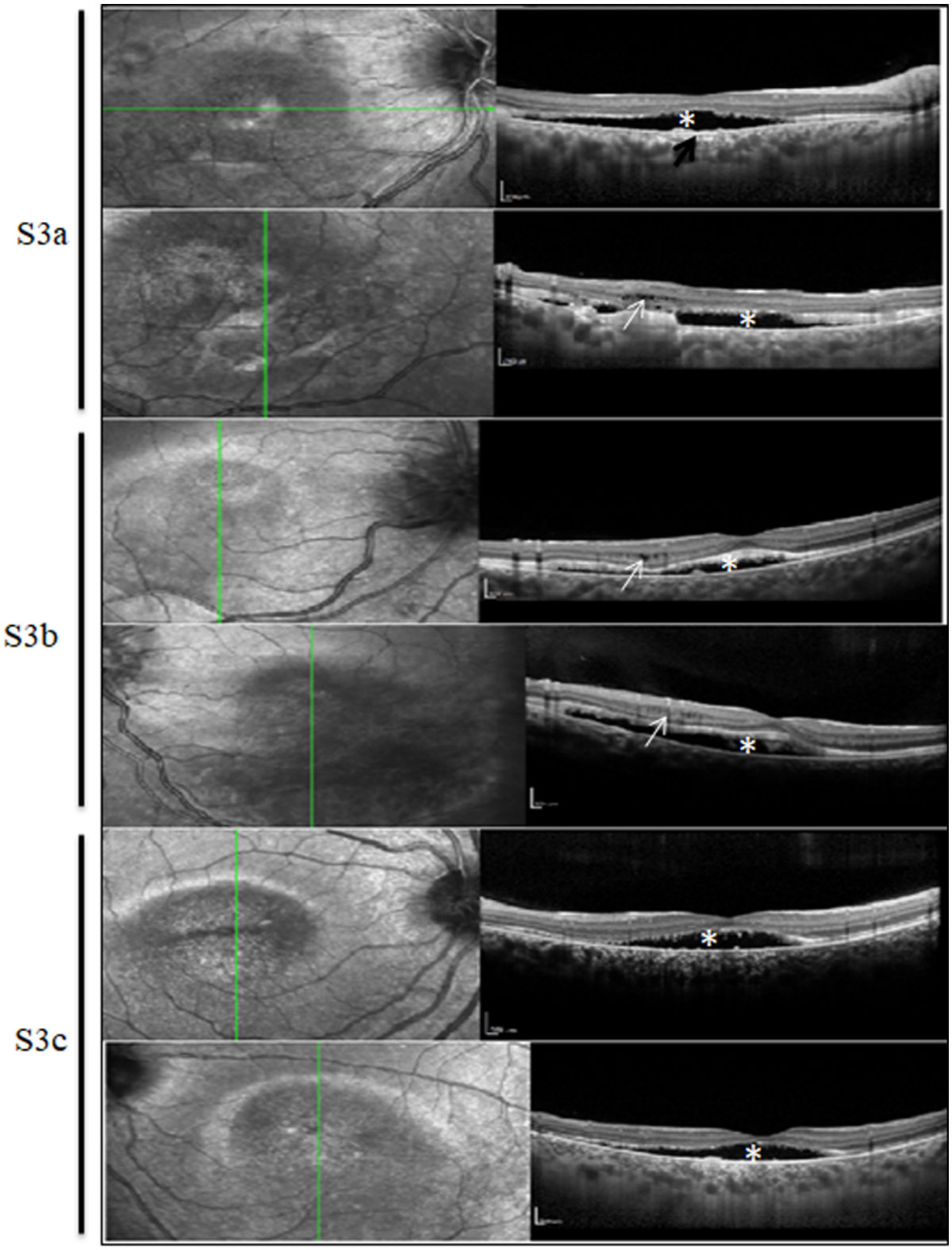
S2c


Right Eye
eogd3a 2013-03-23 13-30-49 Right
Pre-Adaptation
Dark Phase
Bright Phase
20 µV
0
5
10
15
20
25
30 min
Arden Ratio = 1.200
Time to Peak = 6.9 min

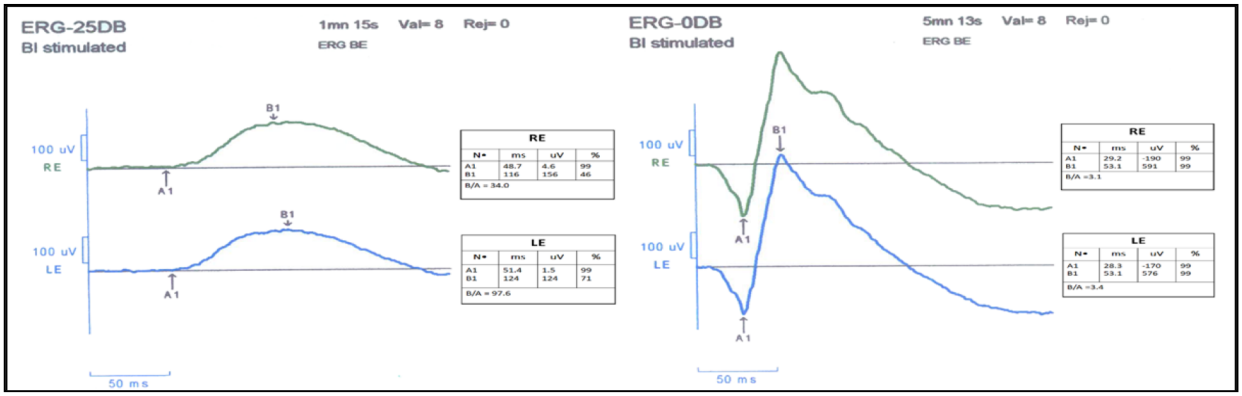
S2d


Left Eye
eogd3a 2013-03-23 13-30-49 Left
Pre-Adaptation
Dark Phase
Bright Phase
20 µV
0
5
10
15
20
25
30 min
Arden Ratio = 1.538
Time to Peak = 10.7 min

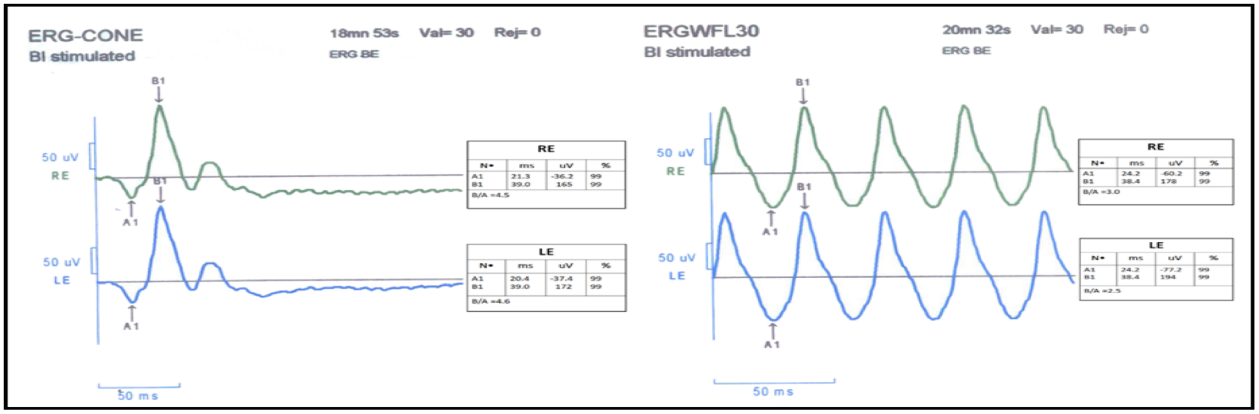
Supplementary Figure S3



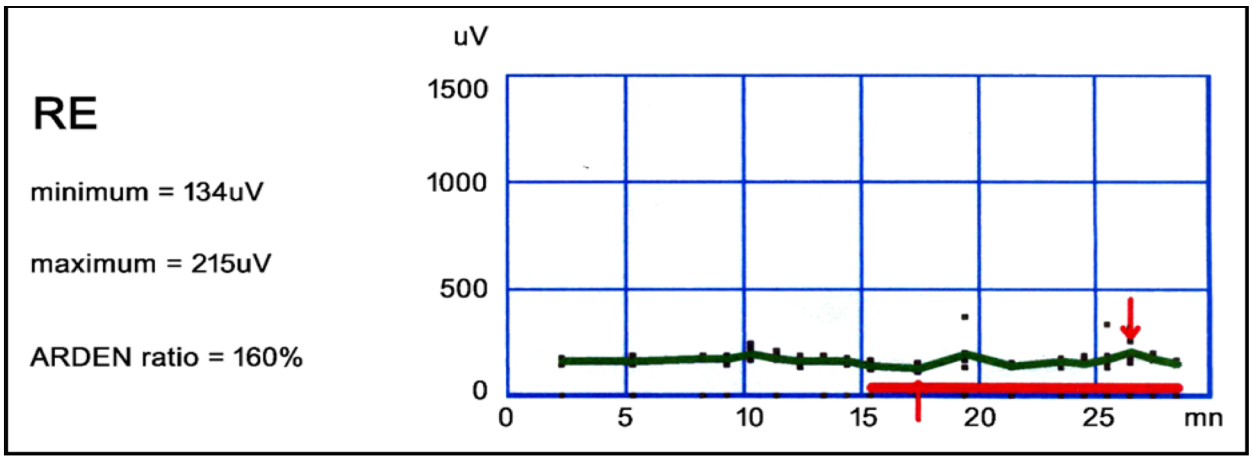
S3d



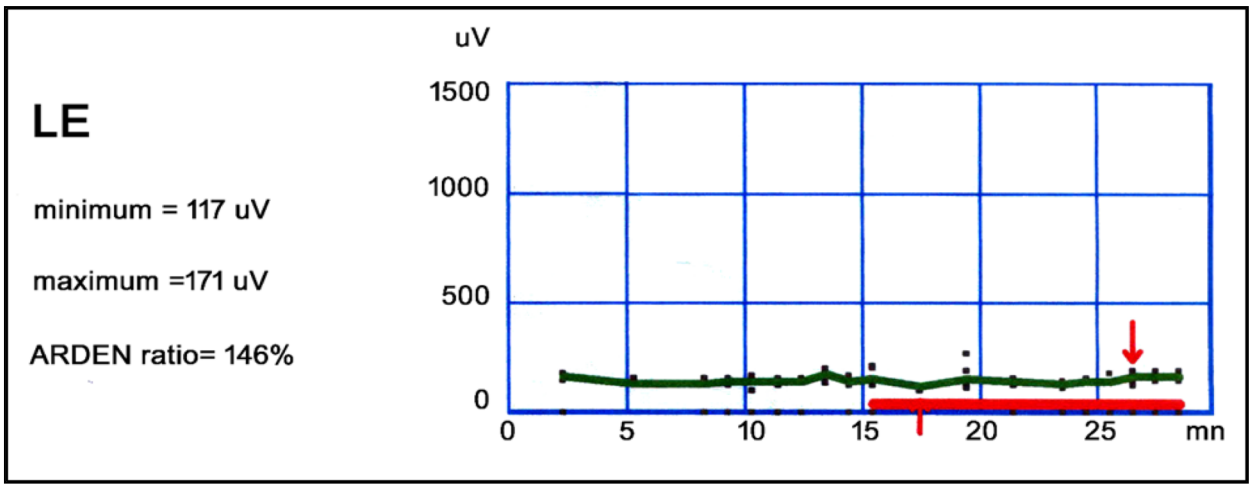
S3e



S3f

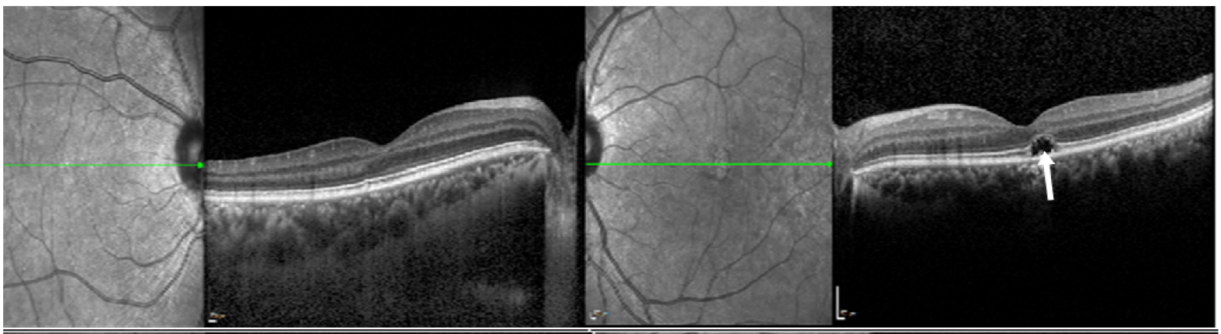


S3g

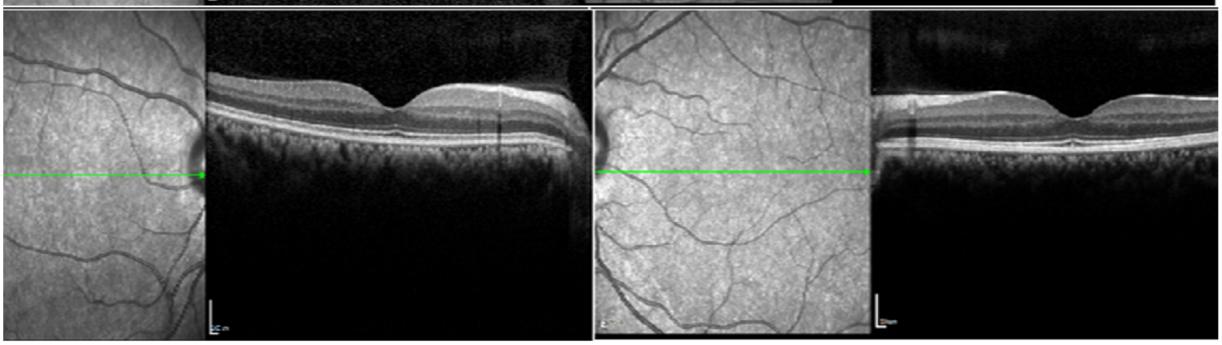


Supplementary Figure S4

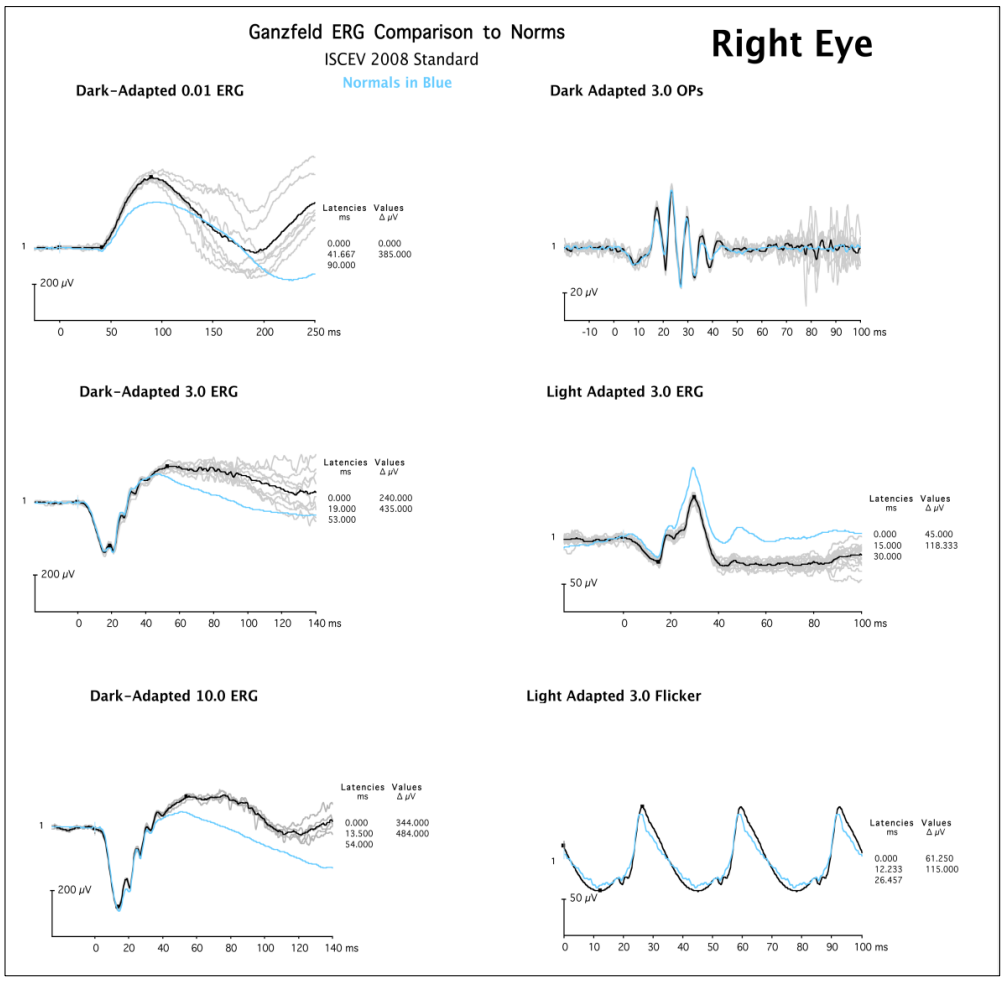
S4a



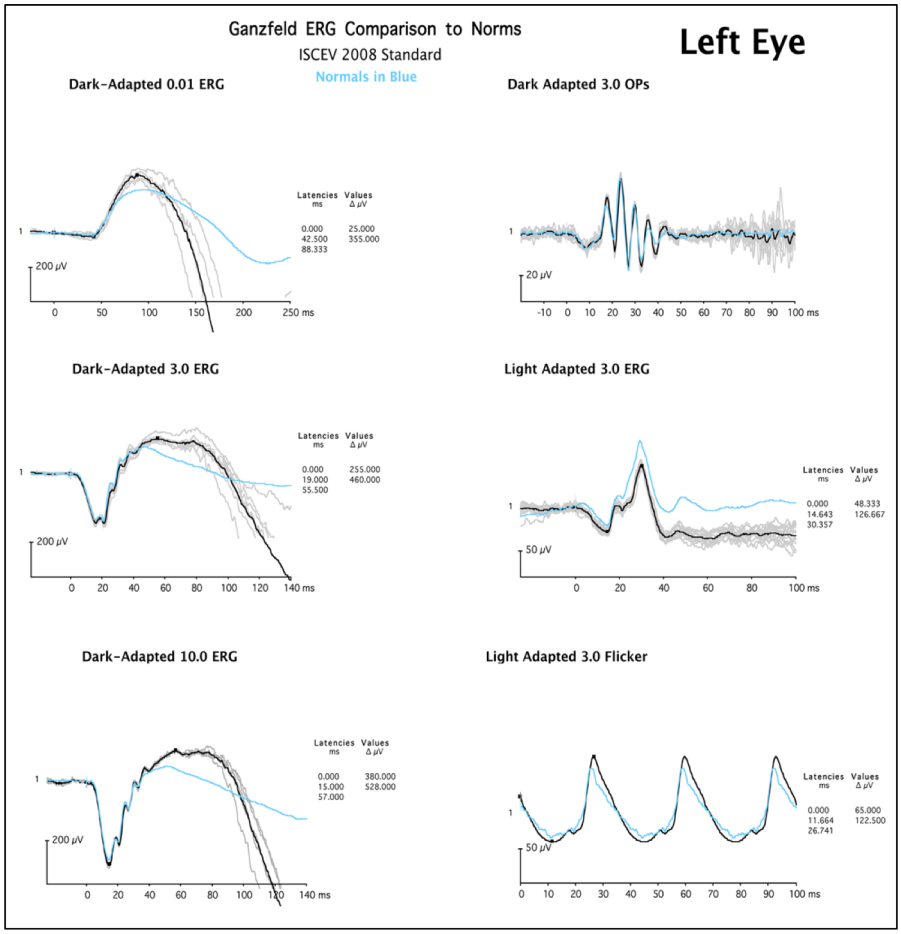
S4b



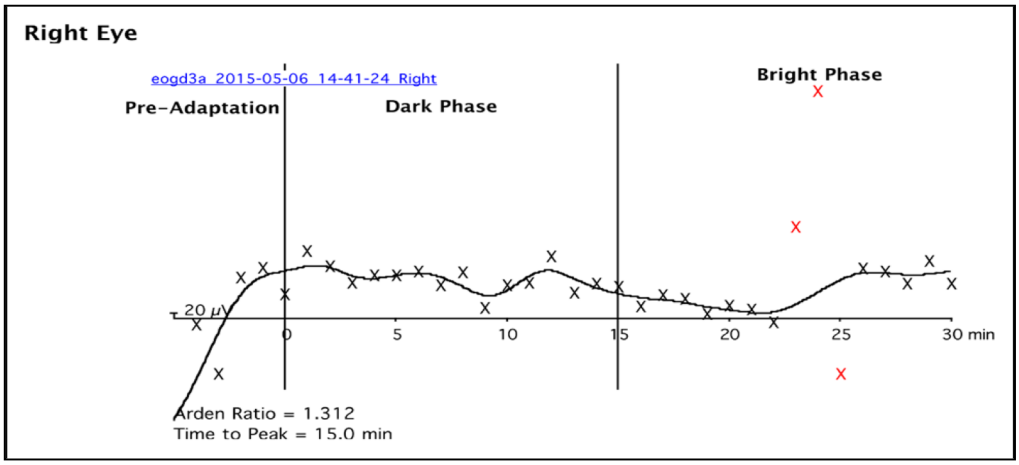
S4c



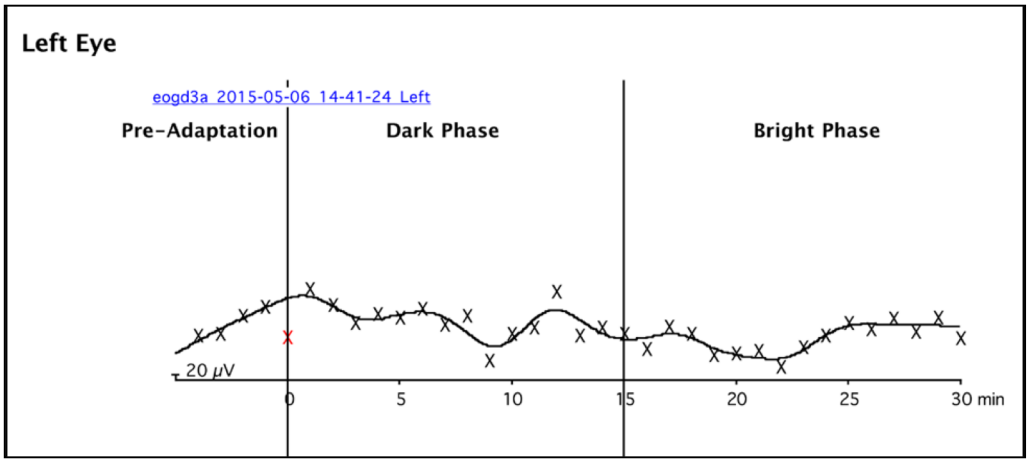
S4d


Ganzfeld ERG Comparison to Norms
ISCEV 2008 Standard
Normals in Blue
Left Eye
Dark-Adapted 0.01 ERG
Dark Adapted 3.0 OPs
Dark-Adapted 3.0 ERG
Light Adapted 3.0 ERG
Dark-Adapted 10.0 ERG
Light Adapted 3.0 Flicker

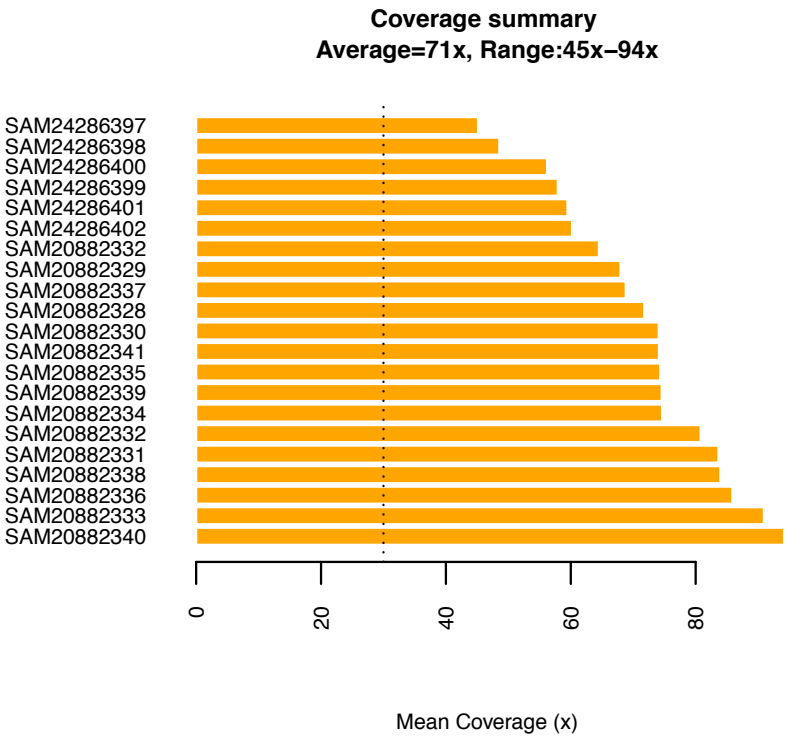
S4e

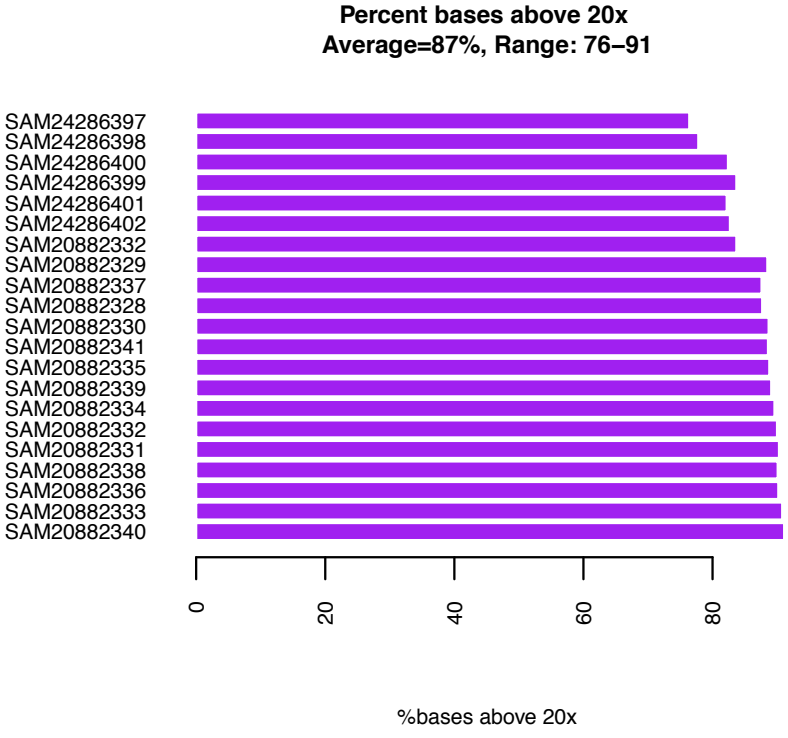

Right Eye
eogd3a_2015-05-06_14-41-24_Right
Pre-Adaptation
Dark Phase
Bright Phase
20 µV
0
5
10
15
20
25
30 min
Arden Ratio = 1.312
Time to Peak = 15.0 min

S4f

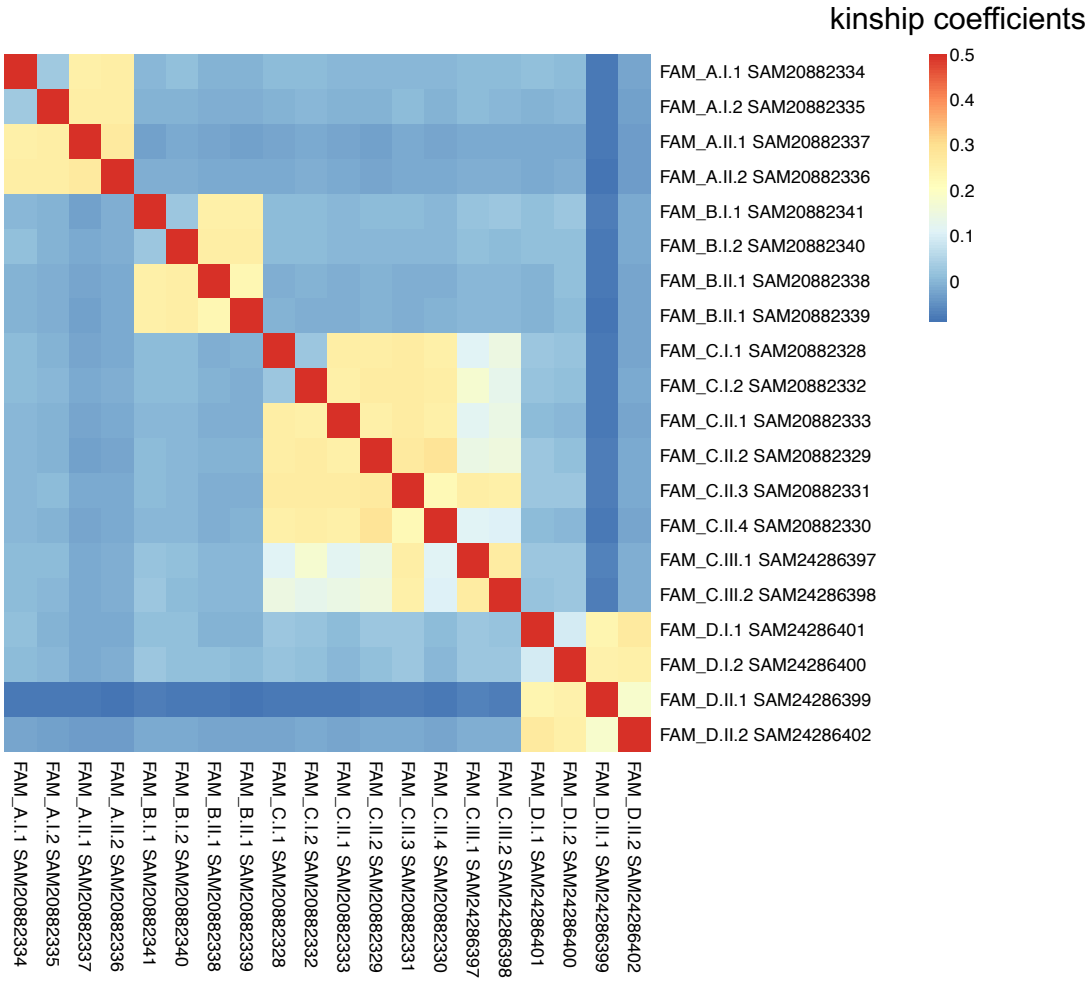

Left Eye
eogd3a_2015-05-06_14-41-24_Left
Pre-Adaptation
Dark Phase
Bright Phase
20 µV
0
5
10
15
20
25
30 min

Supplementary Figure S5

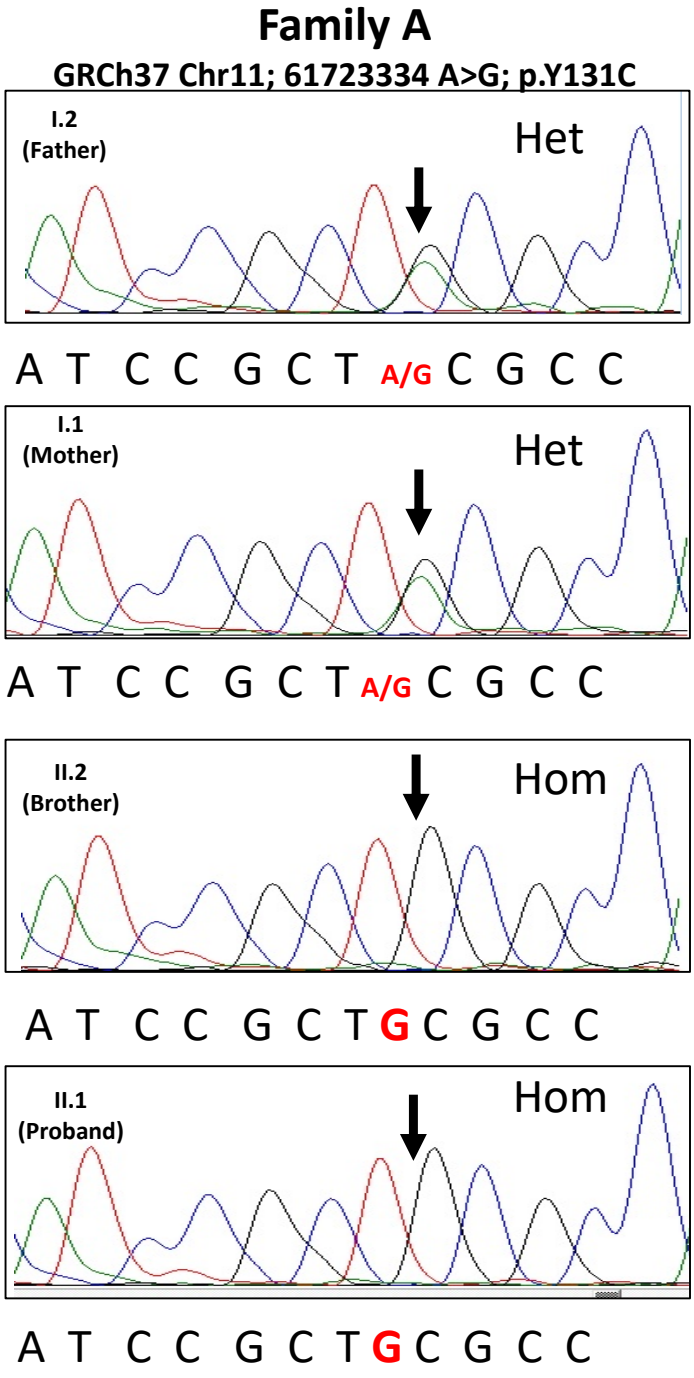




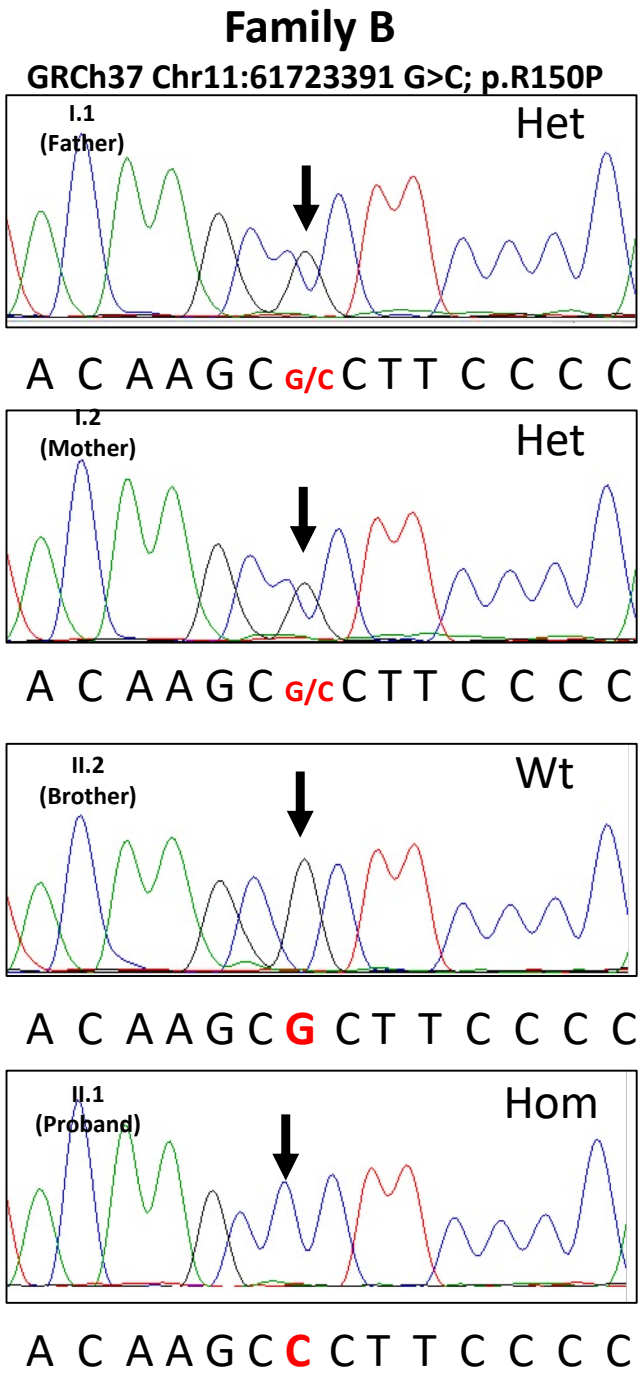
Supplementary Figure S6



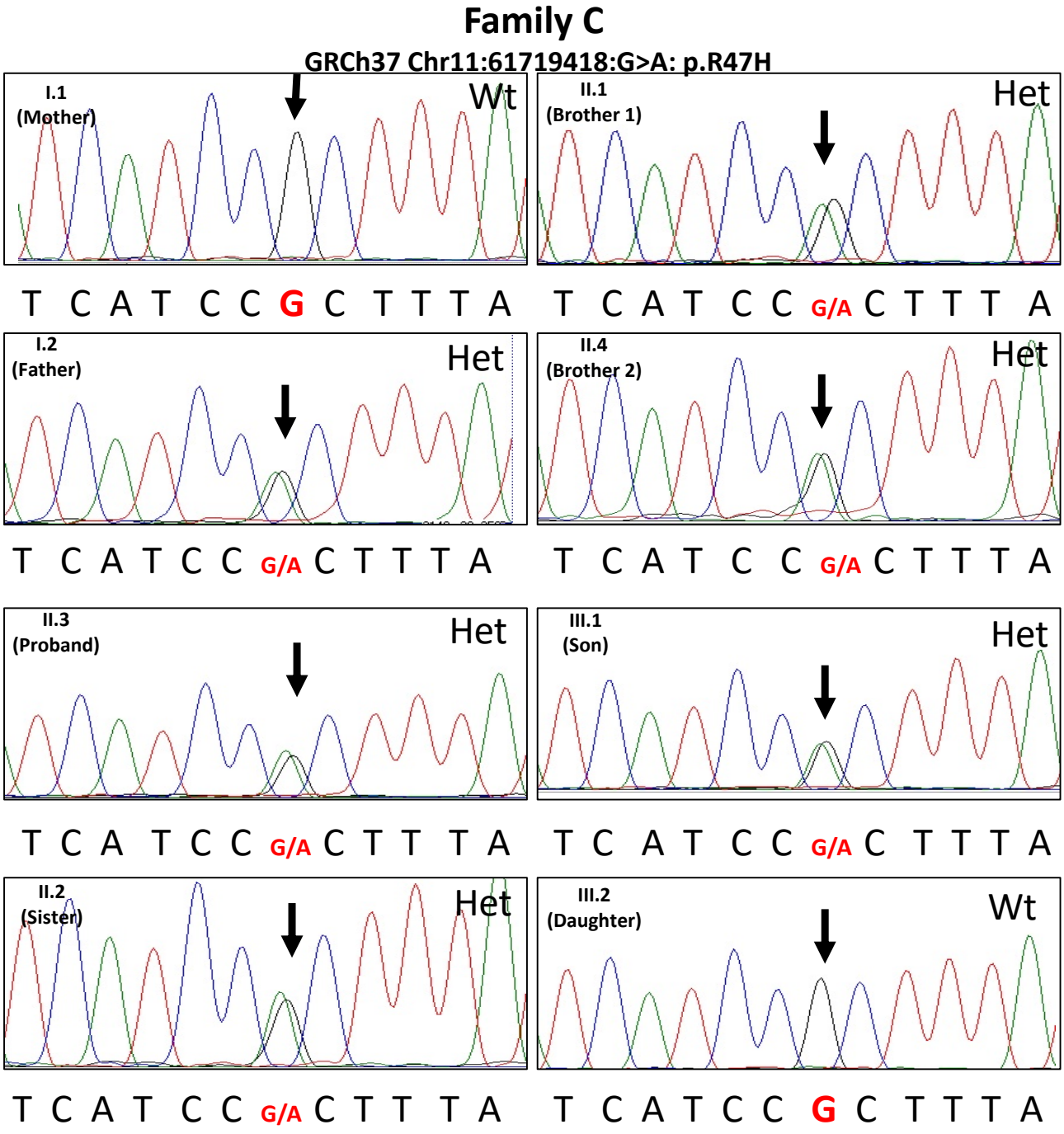
Supplementary Figure S7



Supplementary Figure S8



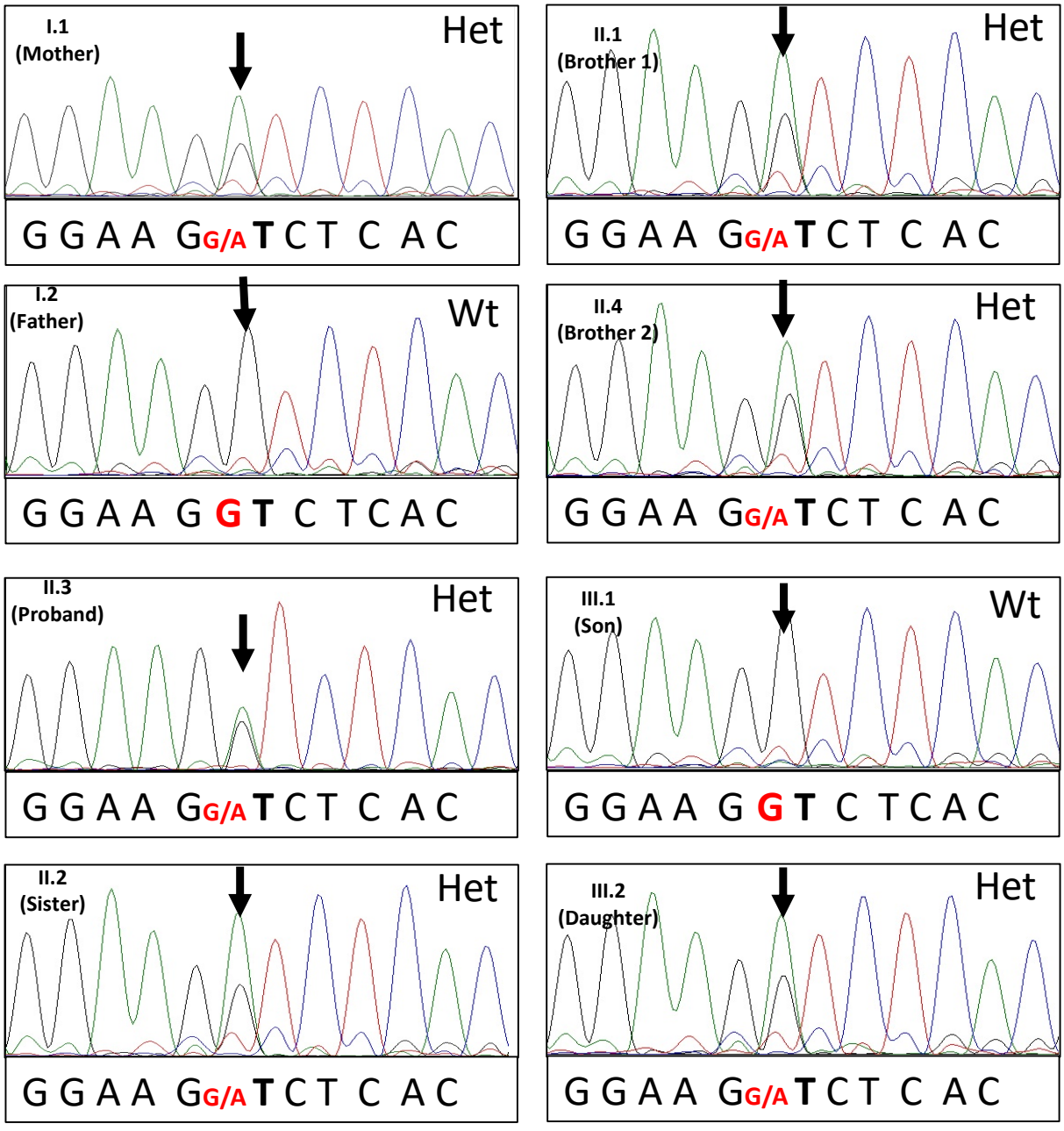
Supplementary Figure S9



Supplementary Figure S10

Family C

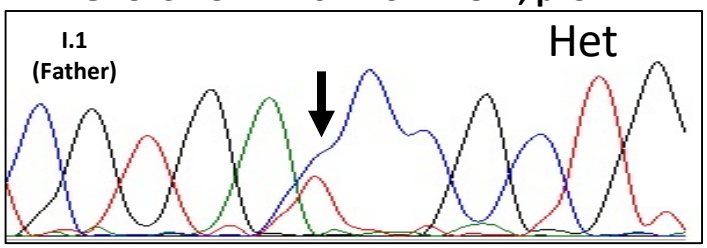
GRCh37 Chr11:61725867:G>A; p.V216I



Supplementary Figure S11

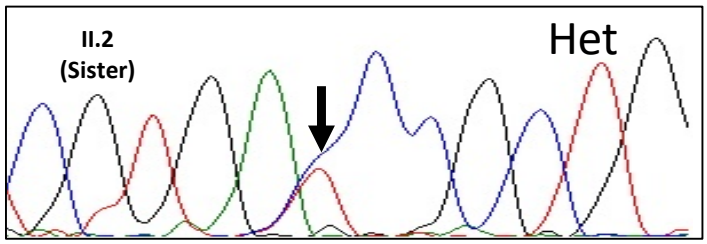
Family D

GRCh37 Chr11: 61723214 C>T; pT91I

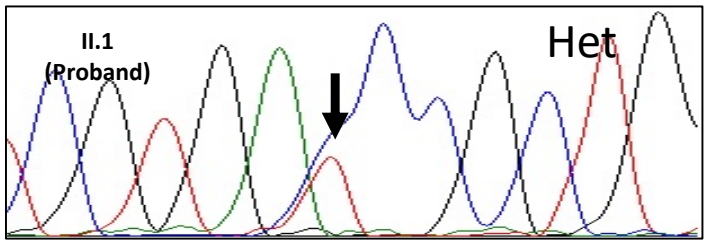


C G T G A C/T C C G C T G

C G T G A **C** C C G C T G



C G T G A C/T C C G C T G



C G T G A C/T C C G C T G