College of Optometry
UNIVERSITY OF HOUSTON

Monthly FOCUS

LIVE Webinar Series

PowerPoint Lecture Handouts

College of Optometry
UNIVERSITY OF HOUSTON

Monthly FOCUS Live Webinar Series Agenda

Wednesday, November 13, 2024			
6:45 pm to 7:00 pm	**Virtual Conference Entry Period**		
7:00 pm to 7:05 pm	Announcements & CE Credit Overview		
7:05 pm to 7:55 pm	**Diagnosis of Inherited Retinal Diseases Using Genetic Testing In Practice** *Presented by Wendy Harrison, OD, PhD, FAAO*	1 D/T Hour	COPE ID # 93626-SD
7:55 pm to 8:00 pm	Questions & Answer Session/Conclusion		

GENETIC TESTING IN CLINICAL PRACTICE: INTERESTING CASES

WENDY HARRISON OD PHD FAAO

ASSOCIATE PROFESSOR UHCO

GENETICS IN PRACTICE

- Over the last several years, genetic testing in practices has evolved.
- We now have access to data we did not have before.
- Some of it is helpful and some of it is not.
- Today we will explore genetics in practice.

GENETIC TESTING IN RETINAL PRACTICE- AN IMPORTANT DETOUR

- Who should do this, when and how.
- You can do it, hopefully this presentation will help you decide if this is something that will build your practice or not.
- Genetic testing for everyday practice is not new concept but its becoming more and more common.
- The big reason its more common is because of cost. There are free programs to get genetic testing done for patients. It is also available for purchase.

NUTS AND BOLTS

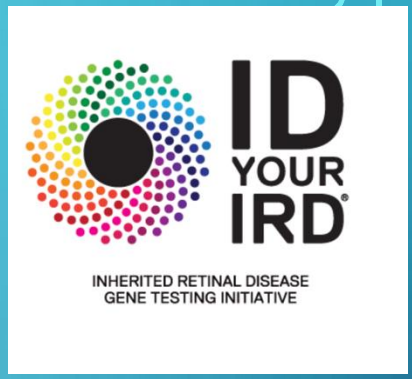
- What do you actually do?

  ordering and programs

  Who qualifies for free

  how to collect spit

NUTS AND BOLTS



- Genetics are generally through prevention genetics for IRDs

- "My retina tracker" is the program through the foundation for fighting blindness and spark therapeutics.
- Invitae labs and blueprint have previously hosted the program.
- https://www.invitae.com/en/idyourird/
- You can still go through other labs but the patient will have to pay
- You can pay for genes not included.

YOU NEED TO SIGN UP FOR THE PROGRAM

- To work with Foundation for fighting blindness you need to sign up through their program.
- There is an application and then you have to be approved
- Once approved you can order tests.

My Retina Tracker Genetic Testing Program: Provider Application

The **My Retina Tracker Genetic Testing Program** is a close collaboration between Foundation Fighting Blindness, PreventionGenetics, and InformedDNA that is largely funded through philanthropic donations to the Foundation Fighting Blindness. To date, thousands of participants have undergone genetic testing through this program. With the resulting genotypic data, which is linked with phenotypic data available in the My Retina Tracker Registry (MRTR), **the primary aim of this Program is to describe the genotype-phenotype associations of inherited retinal diseases (IRDs) in Registry participants to benefit patients and the IRD research community**. It also benefits the research, medical, and IRD patient communities by:

- Creating a research-ready cohort of individuals who have consented to receive targeted recruitment notifications sent by the Foundation on behalf of research/clinical partners.
- Enhancing an already robust dataset which can be shared with research/clinical partners to support study feasibility assessments, site selection, cohort identification, and more.
- Addressing patient barriers to IRD genetic testing and genetic counseling access in the United States.
- Allowing health care providers to order the highest quality genetic testing which has historically not been covered by health insurance but may have medical and familial implications.

The My Retina Tracker Program Panel, provided within this program by PreventionGenetics, is a **carefully curated 110-gene panel targeting relevant genes associated with IRDs that account for over 97% of the solved cases in the My Retina Tracker Genetic Testing Program to date.** This panel includes prevalent mitochondrial genes and full RPGR coverage, including the difficult-to-sequence ORF15 region, which is critical in retinitis pigmentosa diagnostics. Familial variant testing is available to blood relatives at no cost to the patient when certain criteria are met.

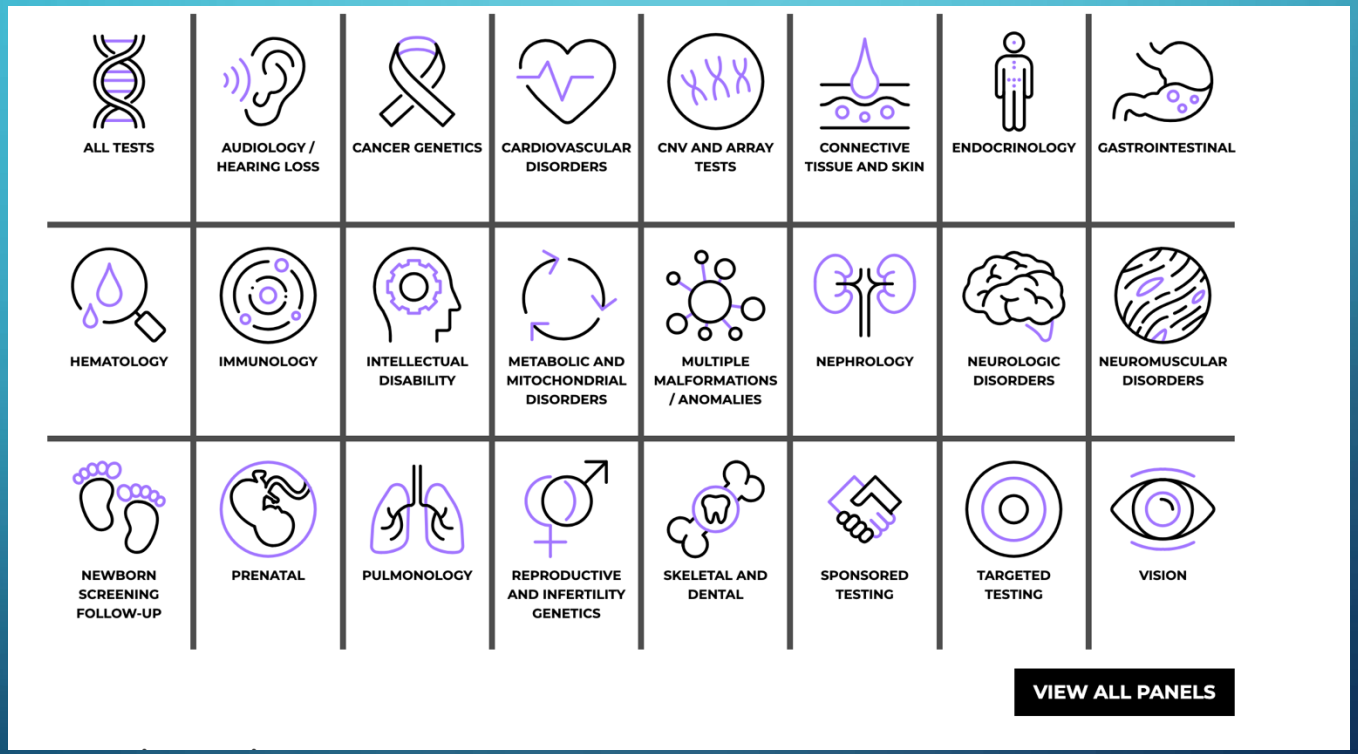
The Foundation also believes that genetic counseling is a critical part of the IRD genetic testing process. Through a partnership with InformedDNA, the Foundation offers genetic counseling to all Program participants undergoing gene panel testing at no cost to the patient. These counseling sessions, which help patients fully understand the medical and familial implications of their results, are conducted in a remote telehealth environment.

Eye care specialists may apply for participation in the My Retina Tracker Genetic Testing Program. As part of the application process, you with be required to agree to the terms and conditions of program use. The application is intended to facilitate the collection of up-to-date information on ordering clinics so we can direct program communications to the correct person and to ensure compliance with program guidelines. The Foundation's Program staff will monitor the results for potential program misuse.

Applications will be reviewed and approved by the My Retina Tracker Genetic Testing Program staff. Upon approval, the Foundation will send you an access code that is required to create a PreventionGenetics ordering portal.

* Required

PREVENTION GENETICS PANEL



My Retina Tracker Program

The My Retina Tracker Genetic Testing Program offers individuals with a clinical diagnosis of an Inherited Retinal Disease (IRD) access to high-quality diagnostic testing, genetic counseling, and connection to a growing IRD registry at no cost to the patient. Targeted familial variant testing is also available to blood relatives of individuals who receive a positive result through the Program. The Foundation Fighting Blindness, a nonprofit organization dedicated to finding treatments for IRD, and Spark Therapeutics sponsor the Program.

MORE INFORMATION

110 GENES INCLUDED:

- https://assets.preventiongenetics.com/sponsoredTesting/ffb/MyRetinaTrackerProgram_110GenePanel.pdf

Test Code: 16023 110 Genes

ABCA4, *ABCC6*, *ABHD12*, *ADGRV1*, *AHI1*, *AIPL1*, *ALMS1*, *BBS1*, *BBS10*, *BBS12*, *BBS2*, *BEST1*, *C1QTNF5*, *CABP4*, *CACNA1F*, *CDH23*, *CDHR1*, *CEP290*, *CEP78*, *CERKL*, *CFAP410*, *CHM*, *CLN3*, *CLRN1*, *CNGA1*, *CNGA3*, *CNGB1*, *CNGB3*, *CNNM4*, *COL18A1*, *COL2A1*, *CRB1*, *CRX*, *CWC27*, *CYP4V2*, *DRAM2*, *EFEMP1*, *ELOVL4*, *EYS*, *FAM161A*, *FLVCR1*, *GUCA1A*, *GUCY2D*, *HGSNAT*, *HK1*, *IFT140*, *IMPDH1*, *IMPG1*, *IMPG2*, *IQCB1*, *JAG1*, *KCNV2*, *KIF11*, *KIZ*, *KLHL7*, *LCA5*, *LRP5*, *MAK*, *MERTK*, *MFSD8*, *MT-ND4*, *MT-ND6*, *MT-TL1*, *MYO7A*, *NMNAT1*, *NPHP1*, *NPHP4*, *NR2E3*, *NRL*, *NYX*, *OAT*, *OPA1*, *PCARE*, *PCDH15*, *PDE6A*, *PDE6B*, *PDE6C*, *PEX1*, *PRDM13*, *PROM1*, *PRPF3*, *PRPF31*, *PRPF8*, *PRPH2*, *PRPS1*, *RAX2*, *RDH12*, *RDH5*, *RHO*, *RLBP1*, *RP1*, *RP1L1*, *RP2*, *RPE65*, *RPGR*, *RPGRIP1*, *RS1*, *SAG*, *SLC24A1*, *SNRNP200*, *SPATA7*, *TIMP3*, *TOPORS*, *TRPM1*, *TSPAN12*, *TTLL5*, *TULP1*, *USH1C*, *USH2A*, and *VPS13B*

Criteria For Test

Participants who undergo genetic testing with the My Retina Tracker Program's 110-gene panel must:

- Reside in the United States or a US territory.
- Have a clinically confirmed diagnosis of an IRD listed below.
- Have no first-degree relatives tested through the Program.
- Have no biological relatives who received informative tests results through the Program.*
- Have not undergone genetic testing with a panel consisting of 32 or more IRD-related genes within the last 5 years, whole exome sequencing, or whole genome sequencing.
- Have not received an IRD-related molecular diagnosis from any previous genetic testing.
- Be willing to join the My Retina Tracker Registry and share their genetic testing results with the Registry.

*Participants with biological relatives who received informative tests results through the Program may qualify for familial variant testing through the My Retina Tracker Program at no cost.

Participants who undergo genetic testing with the My Retina Tracker Genetic Testing Program's targeted familial variant testing must:

- Reside in the United States or a US territory.
- Have a blood relative tested through the Program who received an informative genetic testing result through PreventionGenetics.*
- Have not undergone genetic testing with a panel consisting of 32 or more IRD-related genes within the last 5 years, whole exome sequencing, or whole genome sequencing.
- Have not received an IRD-related molecular diagnosis from any previous genetic testing.
- Be willing to join the My Retina Tracker Registry and share their genetic testing results, including PHI, with the Registry.

*Of note, the familial variants must be sequence-based (nucleotide substitutions and indels) and within the nuclear genome to qualify for free testing and the participant must meet the following criteria based on the inheritance pattern of the gene identified in the proband:

- Dominant conditions: Targeted testing will be available to all blood relatives on the side of the symptomatic parent. If both parents are asymptomatic, targeted parental testing will be offered to determine if the case is a de novo variant. If one of the parents has the variant, targeted testing will be available to all blood relatives on that side of the family.
- Recessive conditions: Targeted testing will be available to all first-degree relatives (parents, full siblings).
- X-linked: Targeted testing will be available to mother, full male siblings, male maternal half-siblings, and male relatives on maternal side. If there is evidence of manifesting heterozygous women in the family history or the literature, targeted testing will be offered through the same pathway as dominant genes.

Eligible inherited retinal degenerative diseases include:

Eligible inherited retinal degenerative diseases include:

- Achromatopsia
- Adult foveomacular vitelliform dystrophy
- Alstrom disease
- Bardet-Biedl syndrome (Laurence-Moon syndrome)
- Best disease
- Bietti crystalline corneoretinal dystrophy
- Choroidal dystrophy
- Choroideremia
- Cohen syndrome
- Cone dystrophy
- Cone monochromacy
- Cone-rod dystrophy
- Congenital stationary night blindness
- Fundus albipunctatus
- Fundus flavimaculatis
- Goldman-Favre vitreoretinal dystrophy (enhanced s-cone syndrome)
- Gyrate atrophy
- Jalili syndrome
- Late-onset retinal degeneration (L-ORD)
- Leber congenital amaurosis
- Macular dystrophy - juvenile inherited only
- Pattern dystrophy
- Refsum syndrome
- Retinitis pigmentosa
- Retinitis pigmentosa atypical
- Retinitis punctata albescens
- Retinoschisis - juvenile
- Rod dystrophy
- Rod monochromacy
- Stargardt disease
- Usher syndrome unspecified
- Usher syndrome - type I
- Usher syndrome - type II
- Usher syndrome - type III

TESTING PANEL

ID YOUR IRD®
INHERITED RETINAL DISEASE GENE TESTING INITIATIVE

Program eligibility

This gene testing initiative is appropriate for patients suspected of having an inherited retinal disease (e.g., retinitis pigmentosa, Leber congenital amaurosis, Stargardt disease, etc.) and who have experienced one or more of the following:

- Peripheral field loss
- Nyctalopia
- Deterioration in color vision
- Central vision loss
- Photophobia
- Any of the above with syndromic findings

Note: This program does not test for genes associated with age-related macular degeneration.

WHAT YOU DO: TAKES ABOUT 10 MINUTES OF EXAM TIME AND 5 ADDITIONAL MIN OF STAFF TIME

- get a kit. They are free.
- Fill out online consent forms. This takes a bit of time.
- Fill out the vile label
- Patient spits in the vile or swab cheek.
- Close it which puts preservative in
- Put vile in bag, bag in box, in fedex bag and mail out with the form.
- Takes about a week to arrive to lab.
- A month or so to get the results.

COMPLEX SCIENCE. STRAIGHTFORWARD PROCESS.

The science behind genetic testing may be deeply complicated, but the testing procedure itself can be relatively simple.

Get an exam.

Meet with a genetic counselor.

Provide a sample.

Discuss the results.

Me??

Eyewanttoknow.com

WHEN TO INCLUDE THE COUNSELOR

- I usually have the genetic counselor call first.
- InformedDNA is the company.
- I follow up afterwards.

WHAT THE RESULTS LOOK LIKE:

RESULT: CARRIER

One Pathogenic variant identified in ABCA4. ABCA4 is associated with autosomal recessive inherited retinal disorders.

One Pathogenic variant identified in IFT80. IFT80 is associated with autosomal recessive asphyxiating thoracic dystrophy.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
ABCA4	c.6320G>A (p.Arg2107His)	heterozygous	PATHOGENIC
IFT80	Deletion (Exons 9-12)	heterozygous	PATHOGENIC
EYS	c.1459+5C>T (Intronic)	heterozygous	Uncertain Significance
NR2E3	c.1127C>T (p.Pro376Leu)	heterozygous	Uncertain Significance
PHYH	c.829-3C>A (Intronic)	heterozygous	Uncertain Significance

Clinical summary

A Pathogenic variant, c.6320G>A (p.Arg2107His), was identified in ABCA4.

- The ABCA4 gene is associated with autosomal recessive cone-rod dystrophy (CRD) (MedGen UID: 349030), Stargardt disease (STGD) (MedGen UID: 383691), and retinitis pigmentosa (RP) (MedGen UID: 400996). Additionally, there is preliminary evidence supporting a correlation with autosomal dominant age-related macular degeneration (ARMD) (PMID: 10880298).
- This individual is a carrier for autosomal recessive ABCA4-related conditions. This result is insufficient to cause autosomal recessive ABCA4-related conditions; however, carrier status does impact reproductive risk.
- ABCA4-related disorders consist of a spectrum of phenotypically overlapping retinal dystrophies (PMID: 26527198, 12789571). CRD is characterized by progressive decreased visual acuity of the central field, photophobia, and poor color vision noted in the first decade of life; night blindness, loss of peripheral vision, and nystagmus also typically occur (PMID: 12037008, 12796258). STGD, also known as fundus flavimaculatus, shows early-stage clinical overlap with CRD, and is characterized by onset of slowly progressive central vision loss in childhood (though first presentation may be in adulthood in STGD); while those affected with STGD do experience night blindness, they typically retain peripheral vision (PMID: 25444351, 21510770). RP initially presents differently from CRD, though they both eventually result in similar clinical phenotypes (PMID: 17270046, 10874631). RP first presents with night blindness and loss of peripheral vision; affected individuals eventually lose central vision (PMID: 26835369, 10874631). RP is highly variable in regards to severity, clinical symptoms, and age of onset (PMID: 17296890).
- Biological relatives have a chance of being a carrier for or being at risk for autosomal recessive ABCA4-related conditions. Testing should be considered if clinically appropriate. The chance of having a child with autosomal recessive ABCA4-related conditions depends on the carrier state of this individual's partner.
- While confirmation of this result by an alternate method could not be completed due to sample limitations, there is high confidence that this variant is a true result.

A Pathogenic variant, Deletion (Exons 9-12), was identified in IFT80.

- The IFT80 gene is associated with autosomal recessive asphyxiating thoracic dystrophy (MedGen UID: 468503).
- This individual is a carrier for autosomal recessive IFT80-related conditions. This result is insufficient to cause autosomal recessive IFT80-related conditions; however, carrier status does impact reproductive risk.
- Asphyxiating thoracic dystrophy (ATD) is a skeletal ciliopathy characterized by shortened ribs and long bones, polydactyly, and brachydactyly (PMID: 22791528, 23339108, 23985472). Extraskeletal clinical features may include retinal dystrophy, renal disease, hepatic fibrosis, and gastrointestinal manifestations (PMID: 22791528, 23339108). ATD may be lethal in the neonatal period due to diminished respiratory capacity from a constricted thoracic cage (PMID: 22791528). For a review of therapeutic methods used in the management of ATD, please refer to Poyner and Bradshaw, 2013 (PMID: 23985472).
- Biological relatives have a chance of being a carrier for or being at risk for autosomal recessive IFT80-related conditions. Testing should be considered if clinically appropriate. The chance of having a child with autosomal recessive IFT80-related conditions depends on the carrier state of this individual's partner.

A Variant of Uncertain Significance, c.1459+5C>T (Intronic), was identified in EYS.

- The EYS gene is associated with autosomal recessive retinitis pigmentosa (RP) (MedGen UID: 350427).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- Familial VUS testing is not offered. Testing family members for this variant will not contribute evidence to allow variant reclassification. Details on our VUS Resolution and Family Variant Testing Programs can be found at https://www.invitae.com/family.

A Variant of Uncertain Significance, c.1127C>T (p.Pro376Leu), was identified in NR2E3.

- The NR2E3 gene is associated with autosomal recessive enhanced S-cone syndrome (ESCS) (MedGen UID: 341446) and autosomal dominant retinitis pigmentosa (RP) (MedGen UID: 410004). Additionally, the NR2E3 gene has preliminary evidence supporting a correlation with autosomal recessive retinitis pigmentosa (RP) (PMID: 18294254, 27032803).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- This variant qualifies for complimentary family studies as part of our VUS Resolution Program. Familial VUS testing is recommended if informative family members are available and are likely to provide additional evidence for future variant reclassification. Details on our VUS Resolution Program can be found at https://www.invitae.com/family.

THE GOOD AND THE BAD OF THIS TESTING

- So here's the issue:

1. The results are often ambiguous
2. I'm not a genetic counselor, even when they are positive I often wonder if what I say is adequate. (do you know what those diseases are? Can you describe them with elegance?)
3. It takes me a lot of time to figure all this out.
4. The same gene can have different presentations
5. Conversations are often long. Take up a lot of chair time.

- Genecard: https://www.genecards.org/cgi-bin/carddisp.pl?gene=IFT80
- OMIM (Online Mendelian Inheritance in Man) : https://omim.org/entry/611177
- https://www.genenames.org/

WHO TO TEST?

- I often get asked about testing family members, children etc.
- My rule of thumb: don't test people without symptoms (they don't qualify for free testing anyway)
- Also there are AMA guidelines for this

AMA GUIDELINES FOR GENETIC TESTING OF CHILDREN

- https://code-medical-ethics.ama-assn.org/ethics-opinions/genetic-testing-children#:~:text=Offer%20diagnostic%20testing%20when%20the,ameliorate%20the%20condition%20are%20available.

MAKING A CLINICAL DIAGNOSIS

- I run an ERG service so I usually use special testing to make diagnosis before running genetics.
- They help provide more information.

ELECTRODIAGNOSTIC TESTING 101

LEANING ON OTHER TEST RESULTS.

I HAVE THE ADVANTAGE OF HAVING AN ERG, MFERG AND/OR VEP ON ALMOST EVERYONE.

THIS ALLOWS ME TO DIAGNOSE BASED ON TESTING AND THEN GO AFTER THE GENETICS.

THIS IS A FULL FIELD ERG

Ganzfeld ERG Comparison to Norms

ISCEV 2008 Standard

Subject Right Eye

Normals

Dark-Adapted 0.01 ERG

fes08RBq2_2014-02-11_14-06-39_Right
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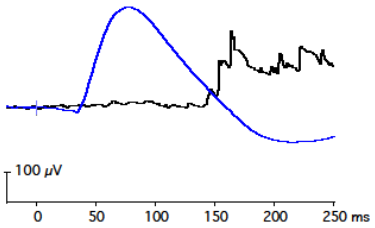
Normals_File10(3,fes08RBq2,Right,C1)



Scotopic 3.0 OPs

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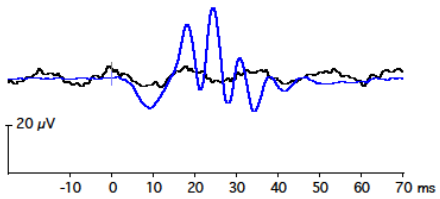
Normals_File10(3,feo08RBq2,Right,C1)



Dark-Adapted 3.0 ERG

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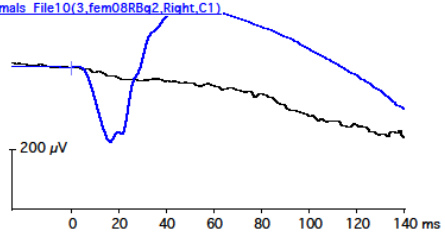

Photopic 3.0 ERG

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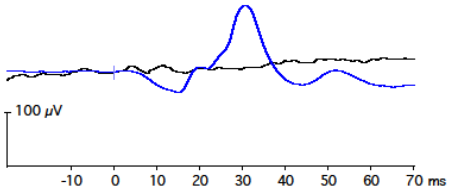
Normals_File10(3,fepww08RBq2,Right,C1)



Dark-Adapted 10.0 ERG

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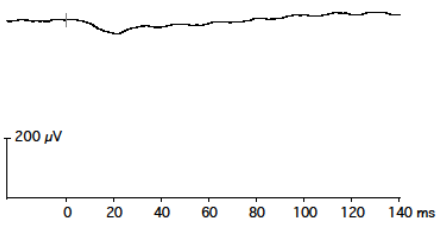
Normal_File(ELeftC1)
Normal_File(ERightC1)



Photopic 3.0 Flicker

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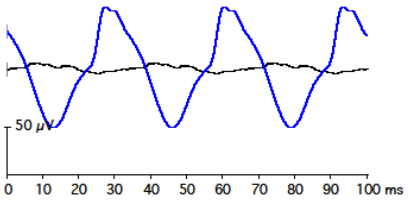
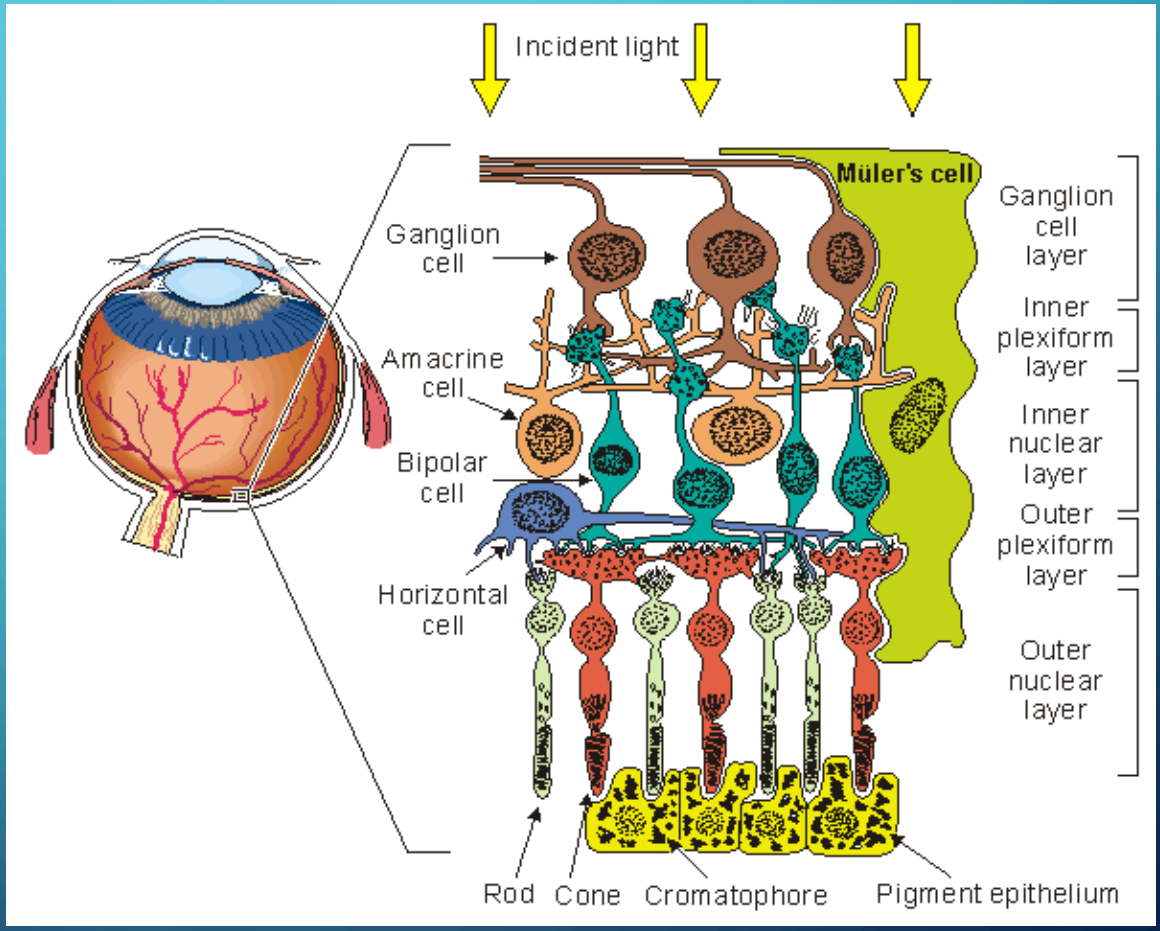


Cellular Origins of Electrodiagnostics

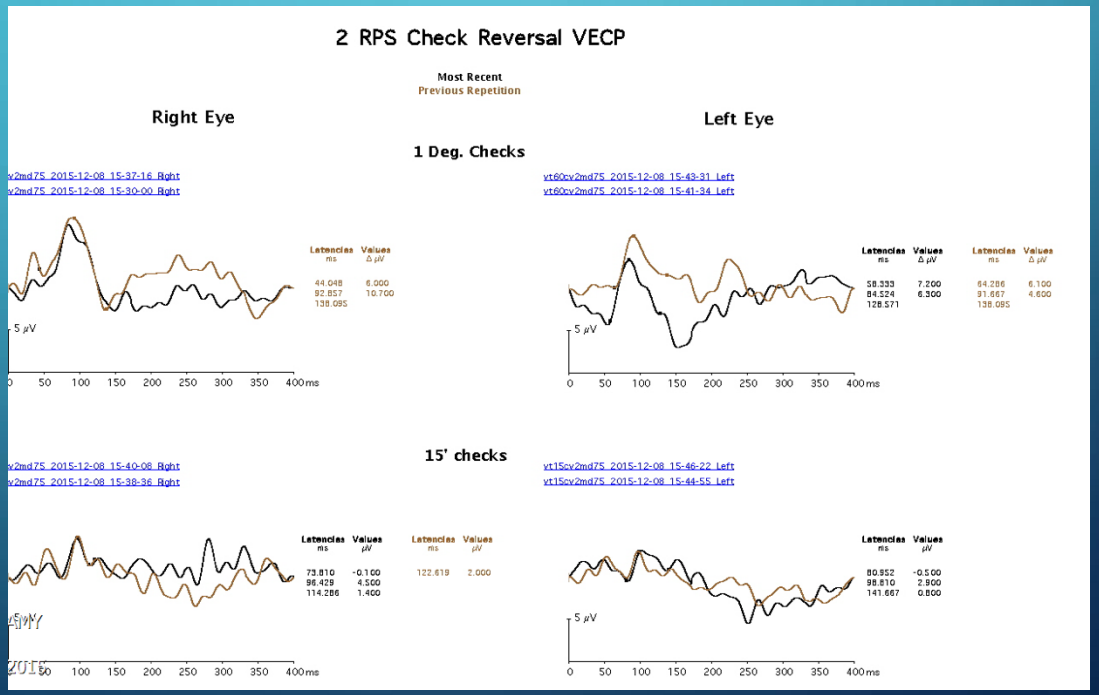
ERG A REVIEW

- Credit: webvision



WHAT DO WE USE IT FOR?

- unexplained vision loss with a normal ERG
- MS
- asymmetric optic nerve atrophy/disease



CASES

- RP
- ABCA4
- other diagnosis

GENETICS IN RP

- Genetics in RP are now a must.
- Becoming Standard of care.

- If you told me 20 years ago that I'd live in Texas and collect spit for a living and talking about spit collection I would not have believed you.

RP CASE WITH GENETICS

- Why must we test the RP patients?

  Treatments available and in trials

RPE65 and Luxturna

RPGR

Others

RPE 65

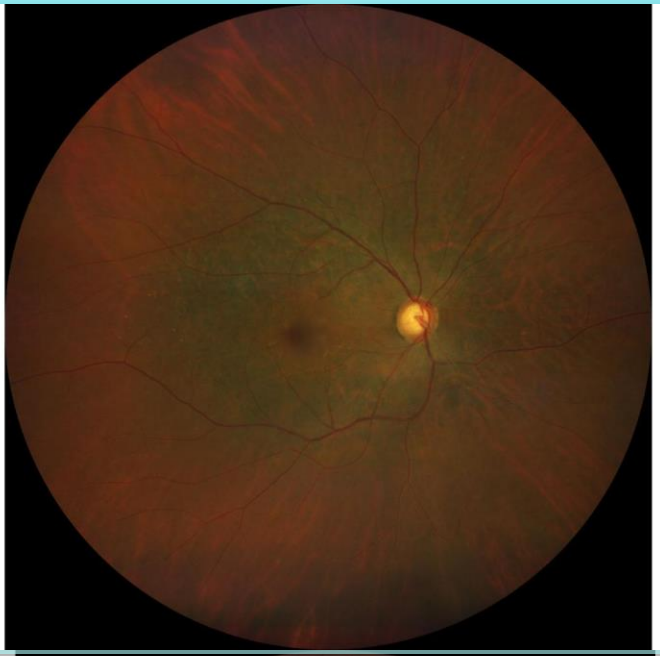
- About 2% of RP
- Also causes LCA
- Luxturna

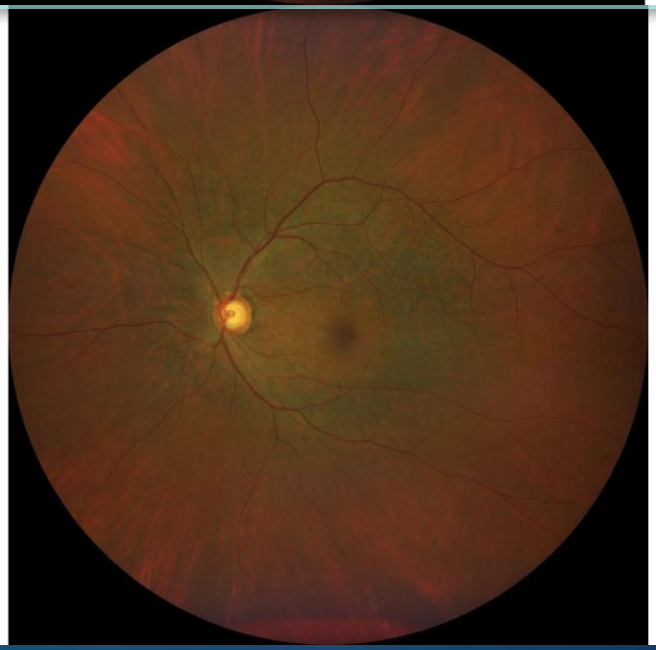
RP CASE 1

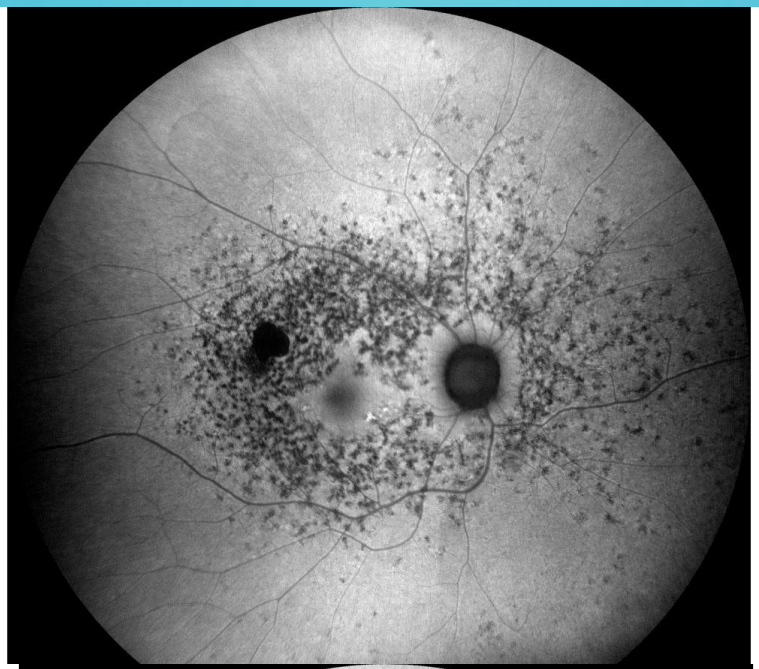
Patient presents for ERG

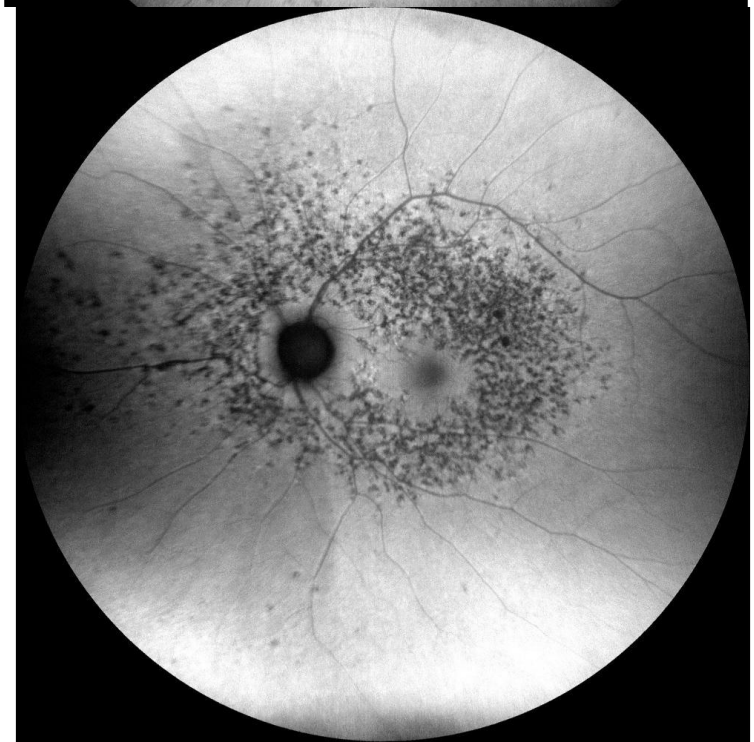
20/20 OD, OS but with sections of lost vision

Lots of the family has RP but retinal appearance doesn't match classic RP



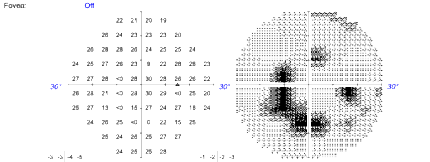


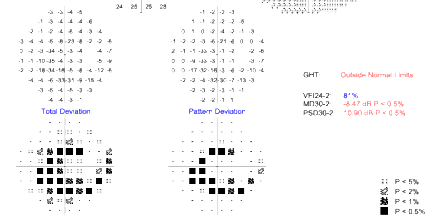




OD Single Field Analysis Central 30-2 Threshold Test

Fixation Monitor:	Gaze/Blind Spot	Stimulus:	III, White	Date:	Jul 18, 2024
Fixation Target:	Central	Background:	31.5 asb	Time:	7:02 AM
Fixation Losses:	0/16	Strategy:	SITA Fast	Age:	57
False POS Errors:	3%	Pupil Diameter:	3.3 mm *		
False NEG Errors:	0%	Visus, Acuity:			
Test Duration:	05:29	Rx:	+4.50 DS		
Fovea:	Off				





GHT Outside Normal Limits

VFI24-2 87 %
MD30-2 -5.47 dB P < 0.5%
PSD30-2 * 0.90 dB P < 0.5%

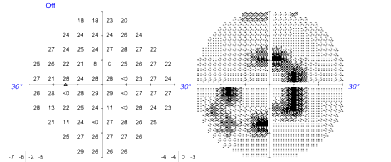
P < 5%
P < 2%
P < 1%
P < 0.5%

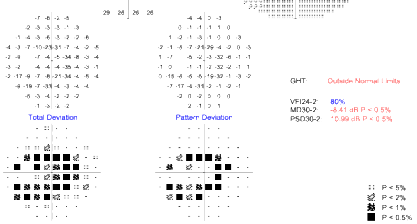
Comments

ZEISS

OS Single Field Analysis Central 30-2 Threshold Test

Fixation Monitor:	Gaze/Blind Spot	Stimulus:	III, White	Date:	Jul 18, 2024
Fixation Target:	Central	Background:	31.5 asb	Time:	7:10 AM
Fixation Losses:	*/16	Strategy:	SITA Fast	Age:	57
False POS Errors:	5%	Pupil Diameter:	4.0 mm *		
False NEG Errors:	*%	Visus, Acuity:			
Test Duration:	06:01	Rx:	+4.00 DS		
Fovea:	Off				





GHT Outside Normal Limits

VFI24-2 80%
MD30-2 -6.41 dB P < 0.5%
PSD30-2 * 0.99 dB P < 0.5%

P < 5%
P < 2%
P < 1%
P < 0.5%

Comments

ZEISS

GENETICS

- Patient was positive for the SAG gene
- SAG is a common RP in the Hispanic population
- Dominant in transmission
- No treatment, following over time.

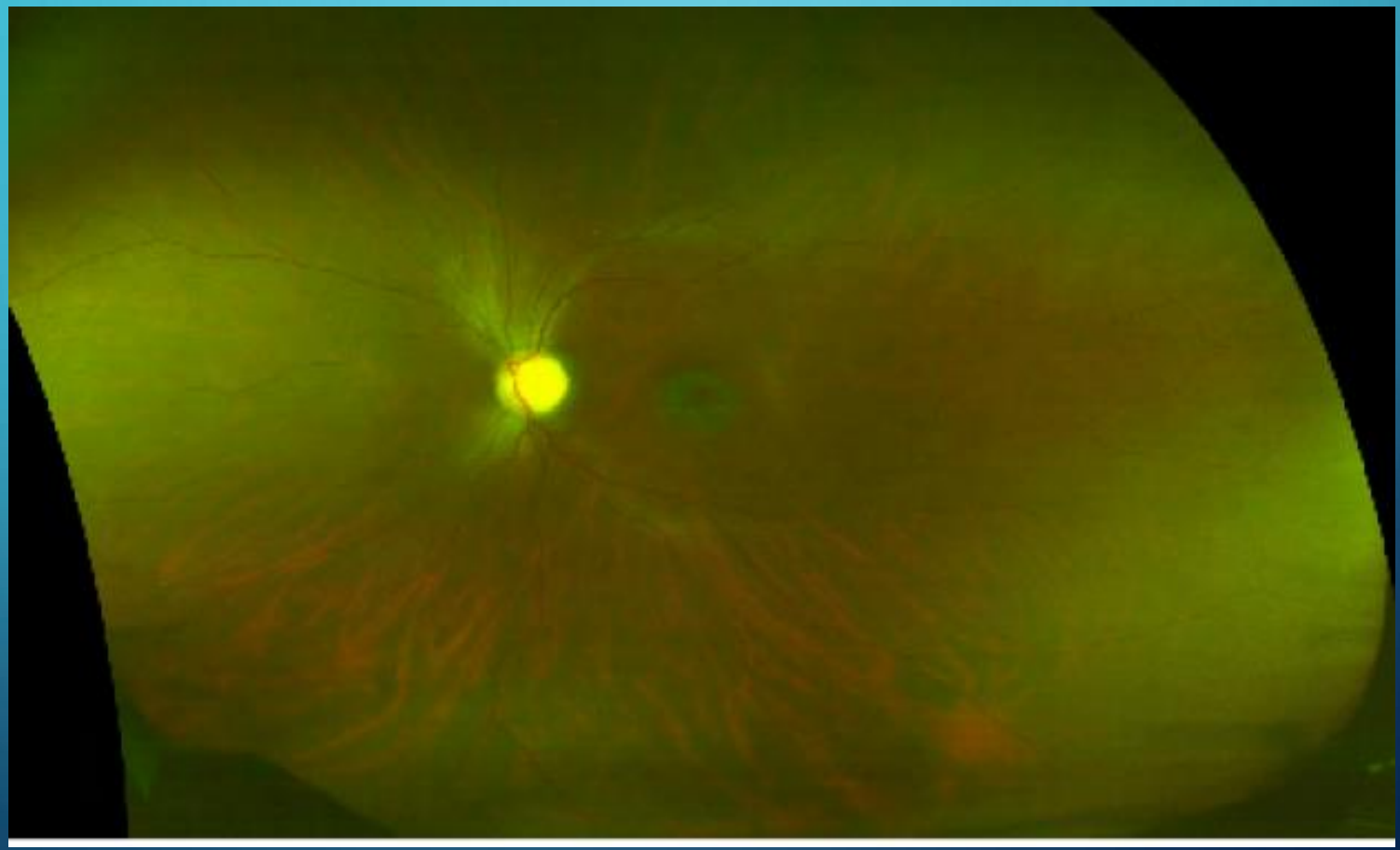
CASE 2- BULLSEYE

- 38 year old BF patient, referred for ERG for a bullseye maculopathy
- Wants more contact lenses. Presented to original OD looking for CL, has been referred to retina and ran out of lenses while waiting.
- No family history of eye problems.
- Does have children
- Was told she was going to lose all her vision. Scared and looking for answers (and also contacts lenses)

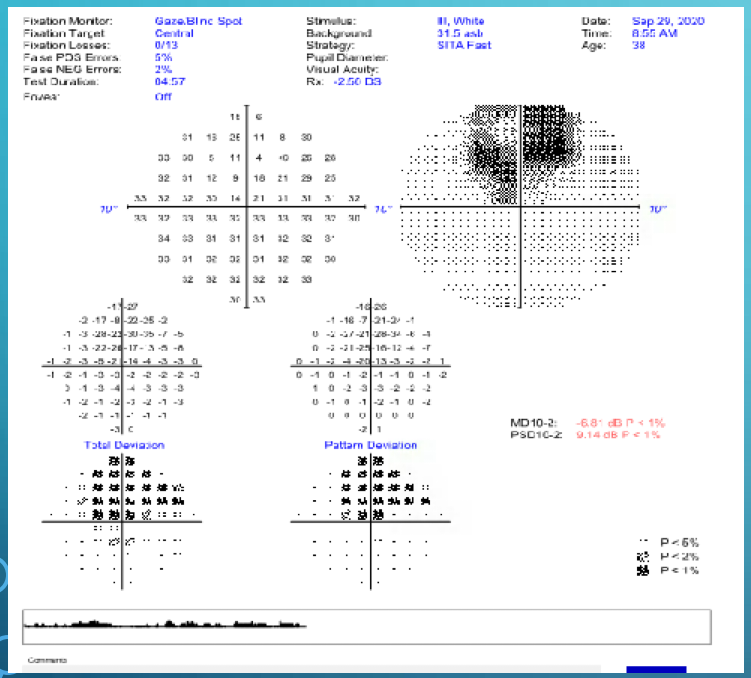
ENTRY TESTS

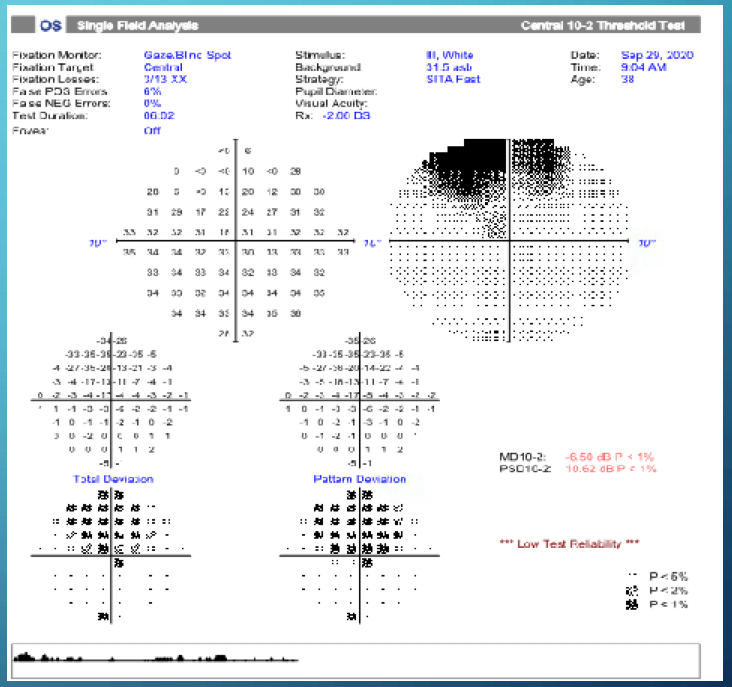
- 20/30 OD 20/80 OS
- Pupils, EOMS normal
- Color: See attached
- Field: See attached

OPTOS

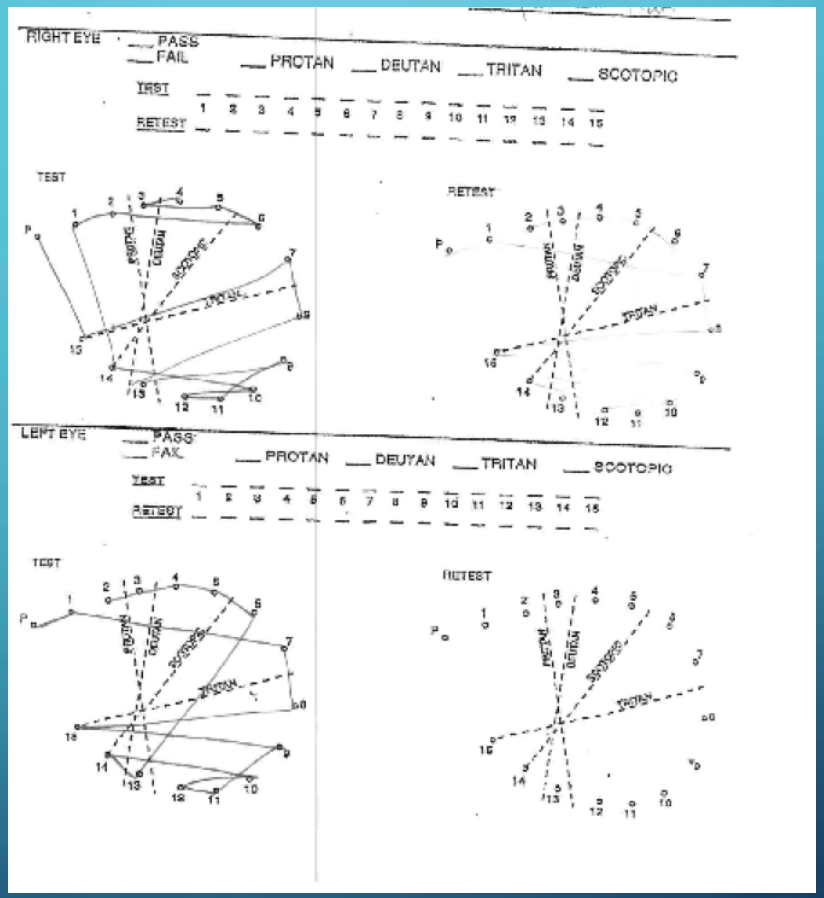


FIELDS

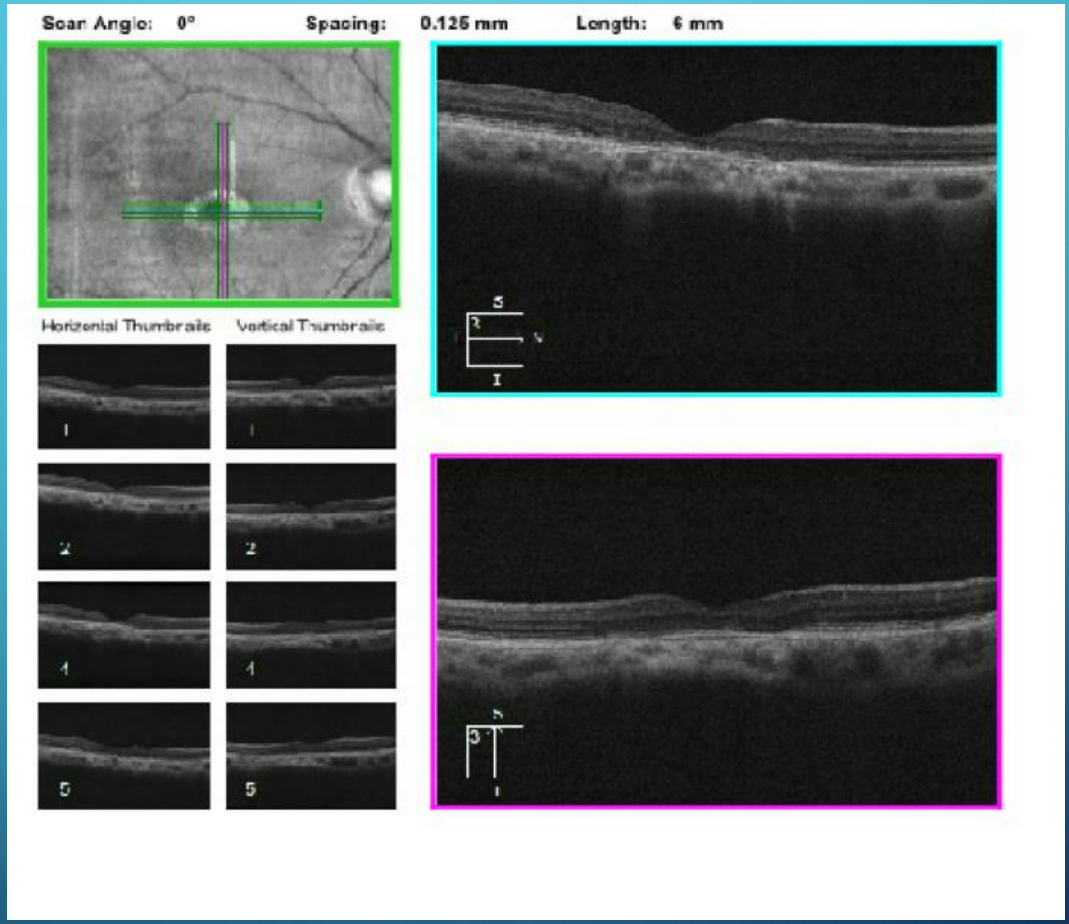

Fixation Monitor: Gaze/Blnc Spot
Fixation Target: Central
Fixation Losses: 0/13
False POS Errors: 5%
False NEG Errors: 2%
Test Duration: 04:57
Fovea: Off
Stimulus: III, White
Background: 31.5 asb
Strategy: SITA Fast
Pupil Diameter:
Visual Acuity:
Rx: +2.50 DS
Date: Sep 29, 2020
Time: 8:55 AM
Age: 38
Total Deviation
Pattern Deviation
MD10-2: -6.81 dB P < 1%
PSD10-2 9.14 dB P < 1%
P < 5%
P < 2%
P < 1%


OS
Single Field Analysis
Central 10-2 Threshold Test
Fixation Monitor: Gaze/Blnc Spot
Fixation Target: Central
Fixation Losses: 3/13 XX
False POS Errors: 6%
False NEG Errors: 0%
Test Duration: 06:02
Fovea: Off
Stimulus: III, White
Background: 31.5 asb
Strategy: SITA Fast
Pupil Diameter:
Visual Acuity:
Rx: +2.00 DS
Date: Sep 29, 2020
Time: 9:04 AM
Age: 38
Total Deviation
Pattern Deviation
MD10-2: -6.58 dB P < 1%
PSD10-2 10.62 dB P < 1%
*** Low Test Reliability ***
P < 5%
P < 2%
P < 1%

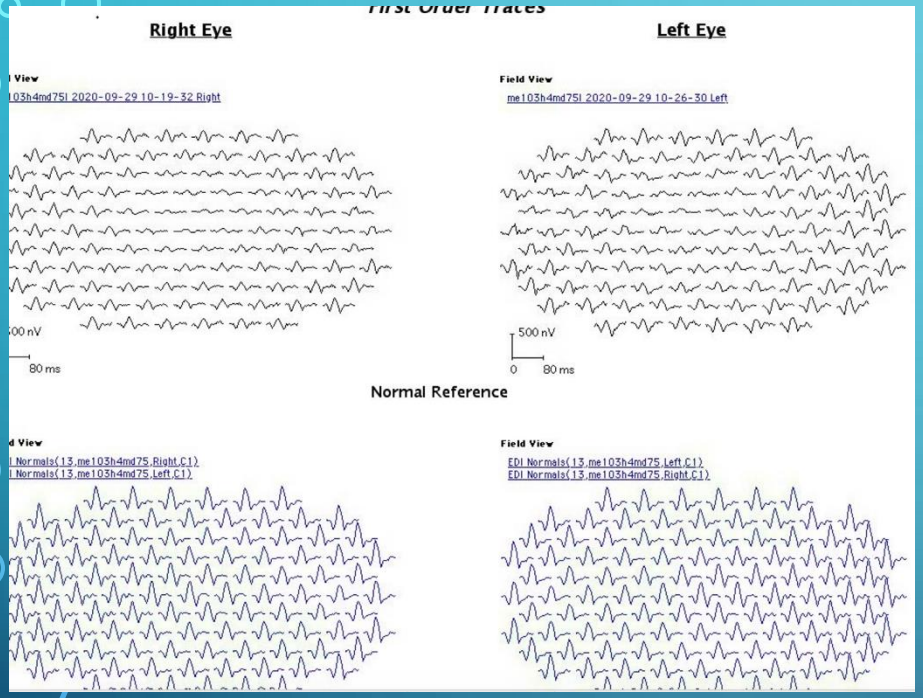
COLOR TESTING

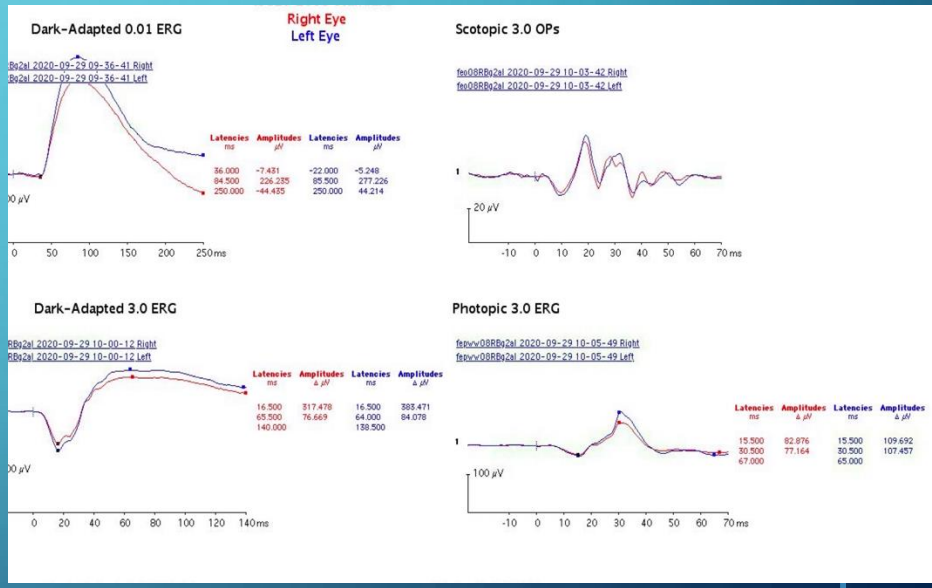


OCT


Scan Angle: 0°
Spacing: 0.125 mm
Length: 6 mm
Horizontal Thumbnails
Vertical Thumbnails

ERGS


First Order Traces
Right Eye
Left Eye
Field View
me103h4md75l 2020-09-29 10-19-32 Right
me103h4md75l 2020-09-29 10-26-30 Left
500 nV
80 ms
0
Normal Reference
Field View
EDI Normals(13,me103h4md75,Left,C1)
EDI Normals(13,me103h4md75,Right,C1)


Dark-Adapted 0.01 ERG
Right Eye
Left Eye
Scotopic 3.0 OPs
Dark-Adapted 3.0 ERG
Photopic 3.0 ERG
Latencies
Amplitudes
20 µV
100 µV

- Exam ends: Cone dystrophy with some rod involvement. Order genetic testing.
- Told patient to expect to lose some more vision in good eye
- Told her its fine to wear CL
- Recommended low vision

GENETIC TESTING RESULTS BACK!

- ABCA4 carrier – one copy of ABCA4 defect
- cone/rod dystrophy. Not 100% clear what is going on but it's likely this gene contributes.

One Pathogenic variant identified in ABCA4. ABCA4 is associated with autosomal recessive inherited retinal disorders.

One Pathogenic variant identified in VPS13B. VPS13B is associated with autosomal recessive Cohen syndrome.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
ABCA4	c.6316C>T (p.Arg2106Cys)	heterozygous	PATHOGENIC
VPS13B	c.5034del (p.His1679Ilefs*8)	heterozygous	PATHOGENIC
COL2A1	c.3511C>T (p.Pro1171Ser)	heterozygous	Uncertain Significance
EMC1	c.1945-1G>T (Splice acceptor)	heterozygous	Uncertain Significance
LRP2	c.12056A>G (p.Gln4019Arg)	heterozygous	Uncertain Significance
MAK	c.556G>T (p.Val186Phe)	heterozygous	Uncertain Significance
WHRN	c.2461A>C (p.Lys821Gln)	heterozygous	Uncertain Significance

A Pathogenic variant, c.6316C>T (p.Arg2106Cys), was identified in ABCA4.

- The ABCA4 gene is associated with autosomal recessive cone-rod dystrophy (CRD) (MedGen UID: 349030), Stargardt disease (STGD) (MedGen UID: 383691), and retinitis pigmentosa (RP) (MedGen UID: 400996). Additionally, there is preliminary evidence supporting a correlation with autosomal dominant age-related macular degeneration (ARMD) (PMID: 10880298).
- This individual is a carrier for autosomal recessive ABCA4-related conditions. This result is insufficient to cause autosomal recessive ABCA4-related conditions; however, carrier status does impact reproductive risk.
- ABCA4-related disorders consist of a spectrum of phenotypically overlapping retinal dystrophies (PMID: 26527198, 12789571). CRD is characterized by progressive decreased visual acuity of the central field, photophobia, and poor color vision noted in the first decade of life; night blindness, loss of peripheral vision, and nystagmus also typically occur (PMID: 12037008, 12796258). STGD, also known as fundus flavimaculatus, shows early-stage clinical overlap with CRD, and is characterized by onset of slowly progressive central vision loss in childhood (though first presentation may be in adulthood in STGD); while those affected with STGD do experience night blindness, they typically retain peripheral vision (PMID: 25444351, 21510770). RP initially presents differently from CRD, though they both eventually result in similar clinical phenotypes (PMID: 17270046, 10874631). RP first presents with night blindness and loss of peripheral vision; affected individuals eventually lose central vision (PMID: 26835369, 10874631). RP is highly variable in regards to severity, clinical symptoms, and age of onset (PMID: 17296890).
- Biological relatives have a chance of being a carrier for or being at risk for autosomal recessive ABCA4-related conditions. Testing should be considered if clinically appropriate. The chance of having a child with autosomal recessive ABCA4-related conditions depends on the carrier state of this individual's partner.

A Pathogenic variant, c.5034del (p.His1679Ilefs*8), was identified in VPS13B.

- The VPS13B gene is associated with autosomal recessive Cohen syndrome (MedGen UID: 78539).
- This individual is a carrier for autosomal recessive Cohen syndrome. This result is insufficient to cause autosomal recessive Cohen syndrome; however, carrier status does impact reproductive risk.
- Cohen syndrome is a developmental disorder characterized by intellectual disability, microcephaly, hypotonia, joint hypermobility, characteristic facial features, short stature, progressive early onset myopia, progressive retinochoroidal dystrophy, neutropenia and truncal obesity developing in late childhood. Affected individuals are described as having a happy disposition. The features of Cohen syndrome can vary widely between individuals (PMID: 12676892).
- Biological relatives have a chance of being a carrier for or being at risk for autosomal recessive Cohen syndrome. Testing should be considered if clinically appropriate. The chance of having a child with autosomal recessive Cohen syndrome depends on the carrier state of this individual's partner.

ABCA4

- Gene for Stargardt
- This is what the genetic counselors will say.

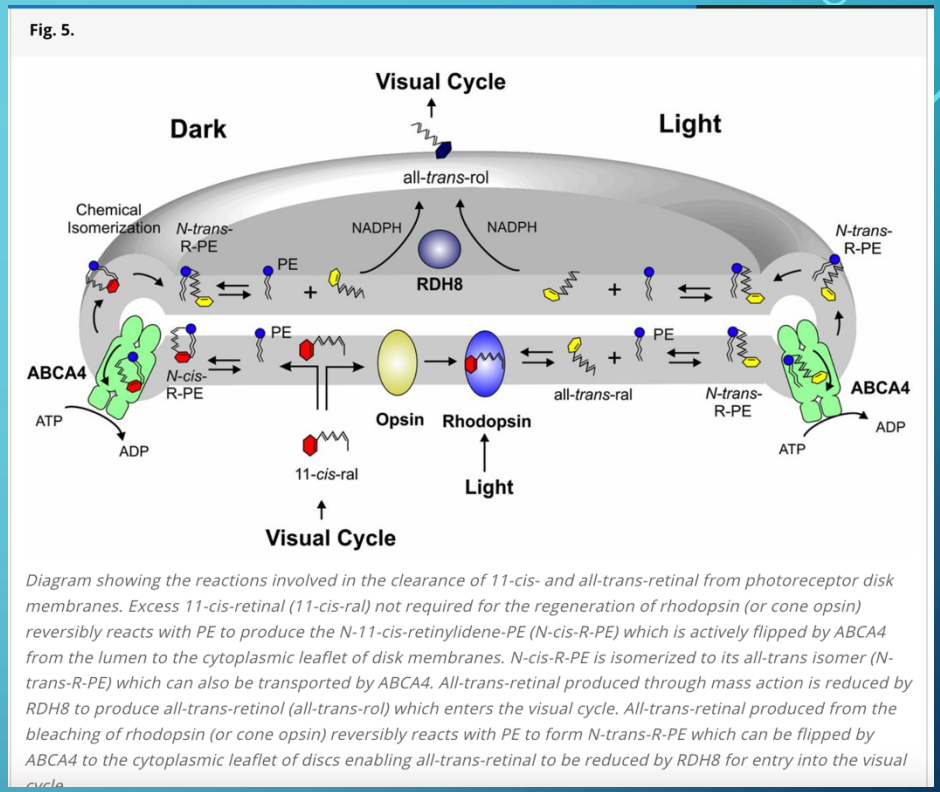
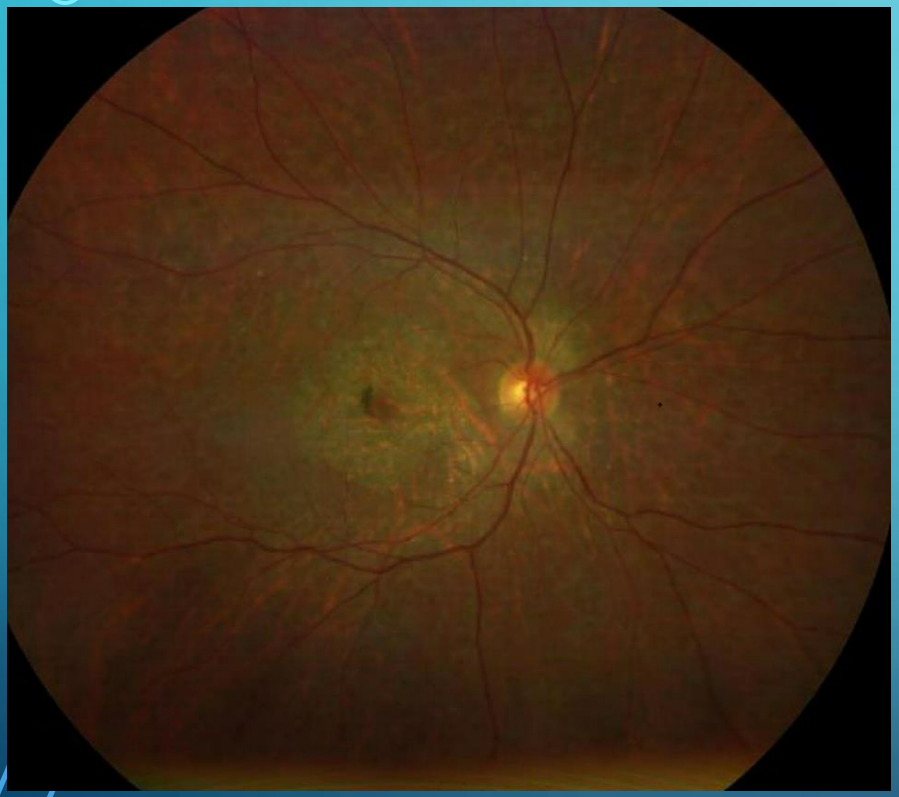
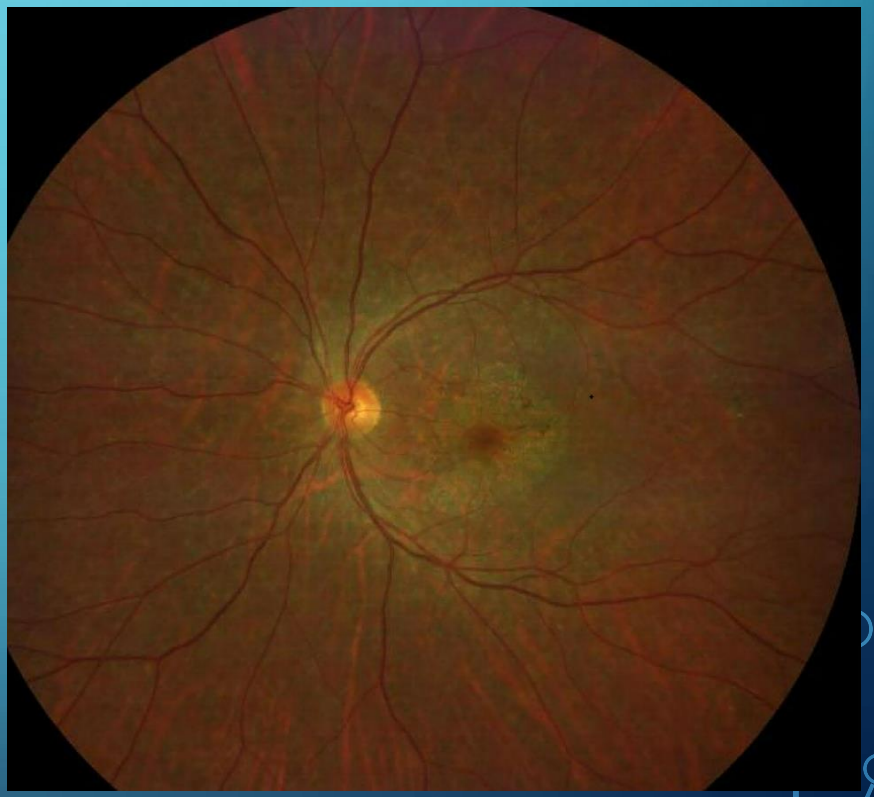


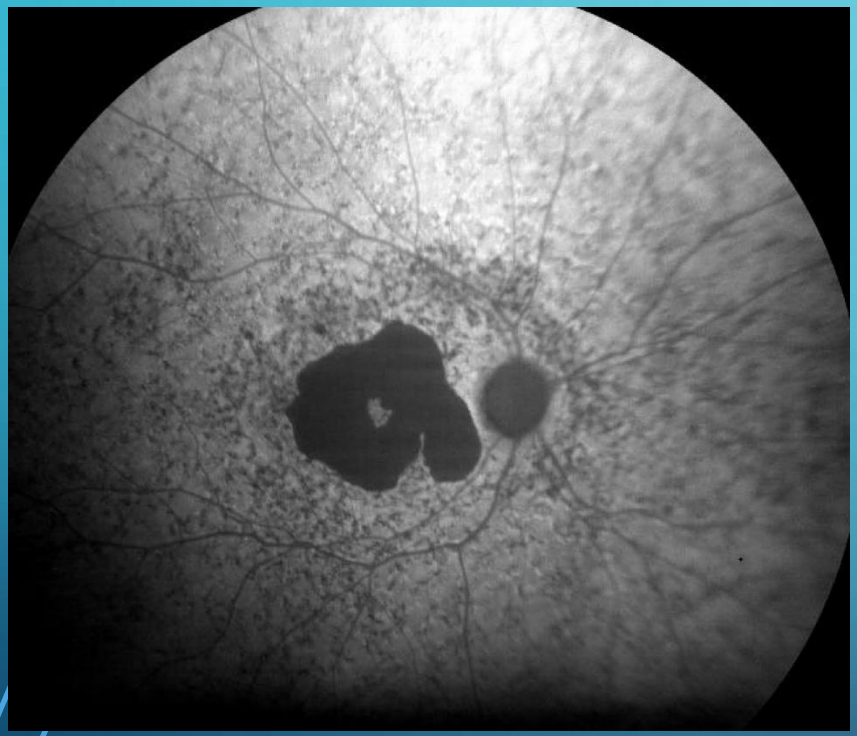
Image from Quazi and Molday PNAS 2014

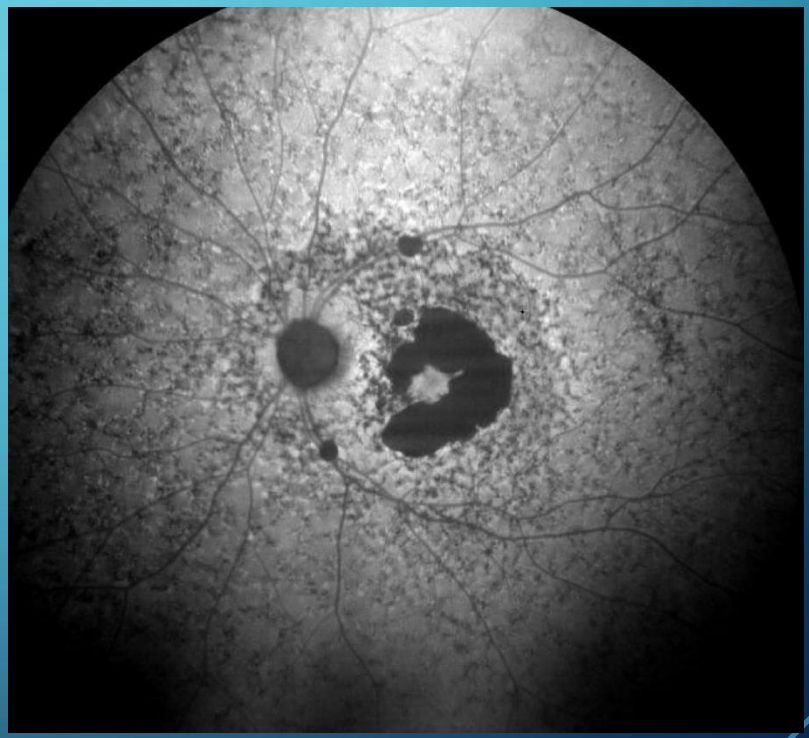
SAME GENE BULLSEYE NEW CASE – CASE 3

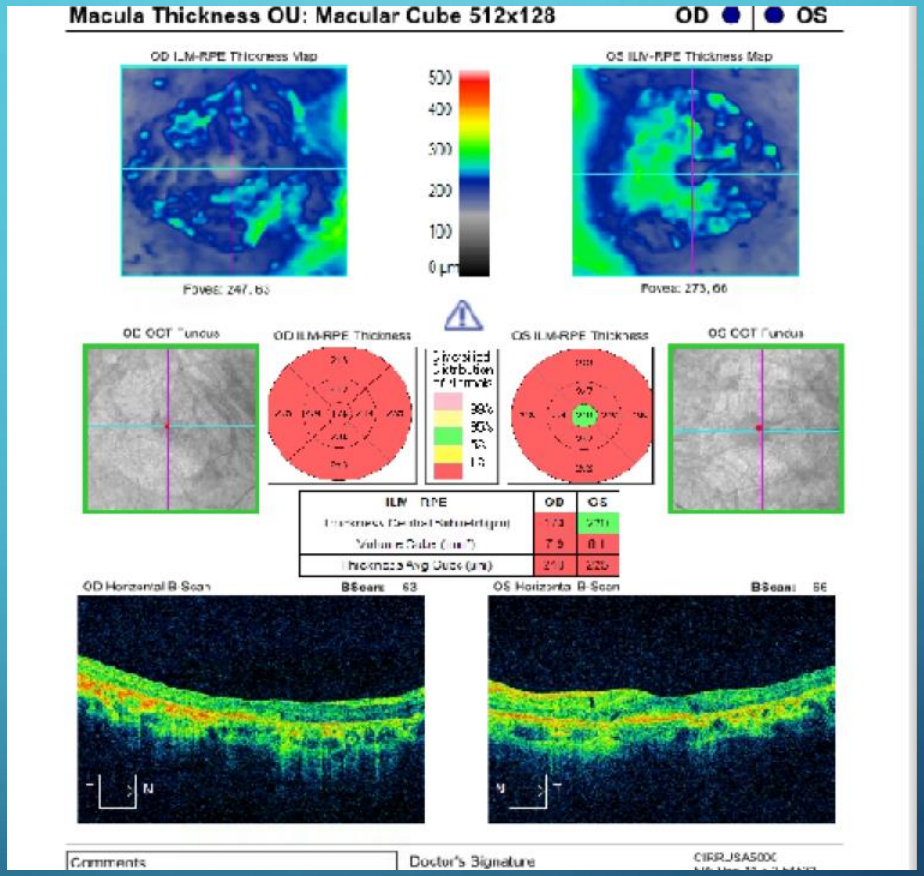
- 49 Asian female referred for ERG/EOG
- 20/60 OD and 20/40 OS
- Loss of central and night vision; exam translated. Patient did not speak English

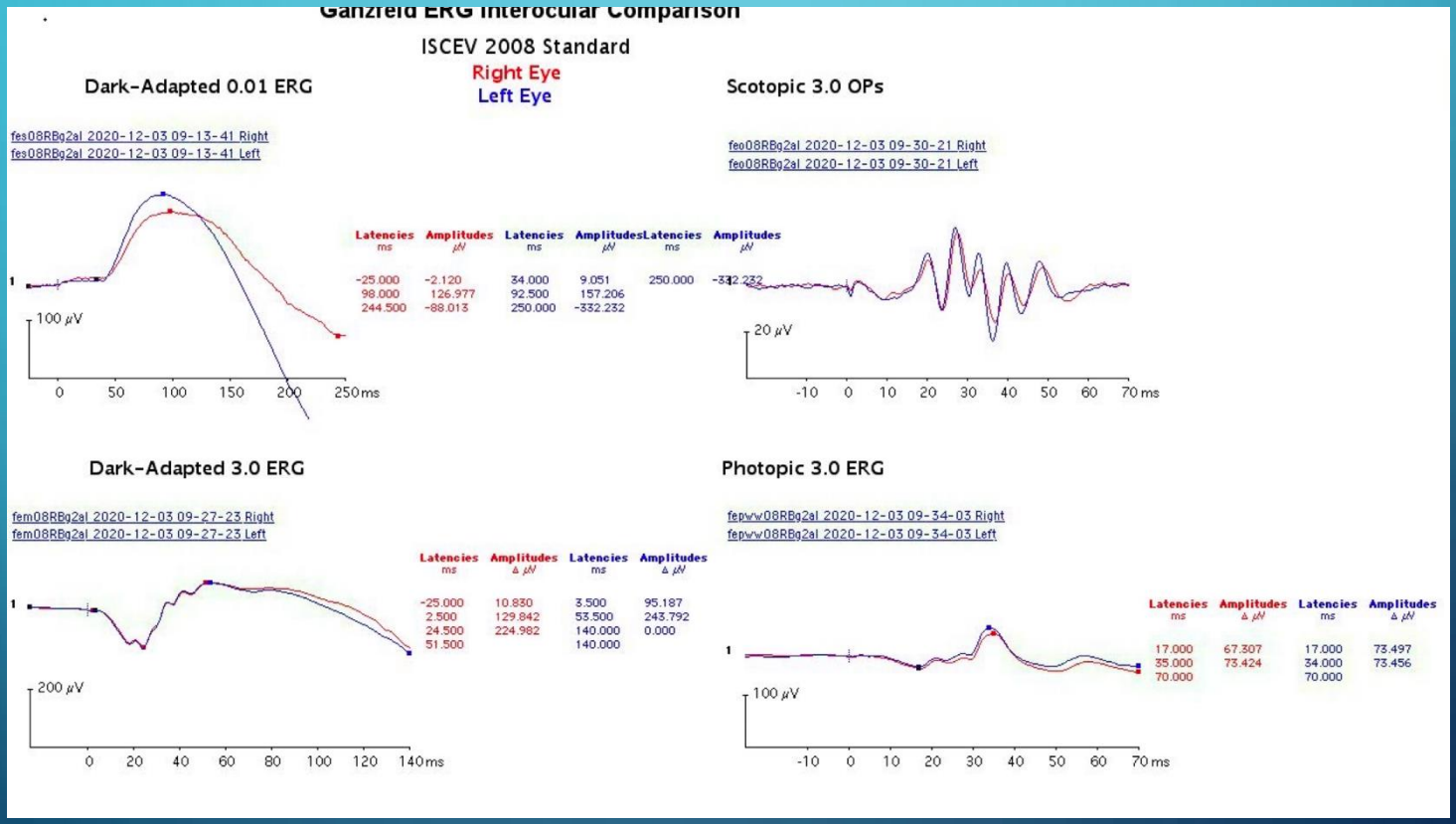









Macula Thickness OU: Macular Cube 512x128
OD
OS
OD ILM-RPE Thickness Map
OS ILM-RPE Thickness Map
500
400
300
200
100
0 µm
Fovea: 247, 63
Fovea: 273, 66
OD OCT Fundus
OD ILM-RPE Thickness
OS ILM-RPE Thickness
OS OCT Fundus
ILM - RPE
OD
OS
OD Horizontal B Scan
BScan: 63
OS Horizontal B Scan
BScan: 56
Comments
Doctor's Signature


Ganzfeld ERG Interocular Comparison
ISCEV 2008 Standard
Right Eye
Left Eye
Dark-Adapted 0.01 ERG
fes08RBg2al 2020-12-03 09-13-41 Right
fes08RBg2al 2020-12-03 09-13-41 Left
Latencies ms
Amplitudes µV
Latencies ms
Amplitudes µV
Latencies ms
Amplitudes µV
-25.000 -2.120 34.000 9.051 250.000 -332.232
98.000 126.977 92.500 157.206
244.500 -88.013 250.000 -332.232
100 µV
0 50 100 150 200 250 ms
Scotopic 3.0 OPs
feo08RBg2al 2020-12-03 09-30-21 Right
feo08RBg2al 2020-12-03 09-30-21 Left
20 µV
-10 0 10 20 30 40 50 60 70 ms
Dark-Adapted 3.0 ERG
fem08RBg2al 2020-12-03 09-27-23 Right
fem08RBg2al 2020-12-03 09-27-23 Left
Latencies ms
Amplitudes Δ µV
Latencies ms
Amplitudes Δ µV
-25.000 10.830 3.500 95.187
2.500 129.842 53.500 243.792
24.500 224.982 140.000 0.000
51.500 140.000
200 µV
0 20 40 60 80 100 120 140 ms
Photopic 3.0 ERG
fepww08RBg2al 2020-12-03 09-34-03 Right
fepww08RBg2al 2020-12-03 09-34-03 Left
Latencies ms
Amplitudes Δ µV
Latencies ms
Amplitudes Δ µV
17.000 67.307 17.000 73.497
35.000 73.424 34.000 73.456
70.000 70.000
100 µV
-10 0 10 20 30 40 50 60 70 ms

RESULT: POTENTIALLY POSITIVE

Two Pathogenic variants identified in ABCA4. ABCA4 is associated with autosomal recessive inherited retinal disorders.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
ABCA4	c.1957C>T (p.Arg653Cys)	heterozygous	PATHOGENIC
ABCA4	c.71G>A (p.Arg24His)	heterozygous	PATHOGENIC
ADGRA3	c.859G>A (p.Asp287Asn)	heterozygous	Uncertain Significance
ALMS1	c.815C>T (p.Ser272Leu)	heterozygous	Uncertain Significance
BBS10	c.2065A>C (p.Thr689Pro)	heterozygous	Uncertain Significance
CEP290	c.1448C>T (p.Thr483Ile)	heterozygous	Uncertain Significance
CNGB1	c.292C>T (p.Pro98Ser)	heterozygous	Uncertain Significance
COL2A1	c.2943C>T (Silent)	heterozygous	Uncertain Significance
COL9A2	c.1736G>A (p.Arg579Gln)	heterozygous	Uncertain Significance
ZNF423	c.1908A>G (Silent)	heterozygous	Uncertain Significance

Two Pathogenic variants, c.1957C>T (p.Arg653Cys) and c.71G>A (p.Arg24His), were identified in ABCA4. The data from this test cannot definitively determine if these variants are on the same or opposite chromosomes.

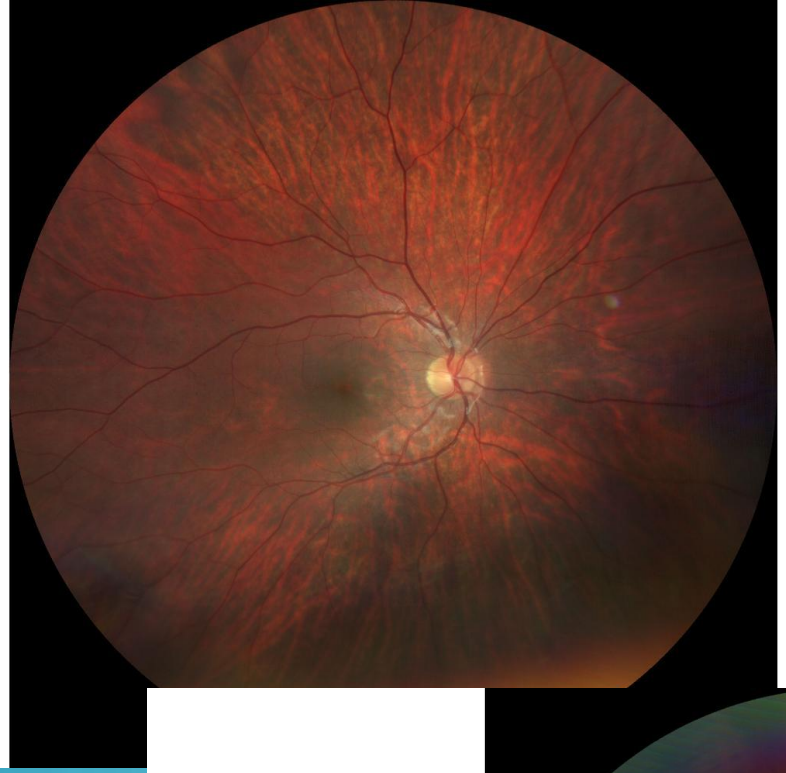
- The ABCA4 gene is associated with autosomal recessive cone-rod dystrophy (CRD) (MedGen UID: 349030), Stargardt disease (STGD) (MedGen UID: 383691), and retinitis pigmentosa (RP) (MedGen UID: 400996). Additionally, there is preliminary evidence supporting a correlation with autosomal dominant age-related macular degeneration (ARMD) (PMID: 10880298).
- If two causative variants are present on opposite chromosomes, then this result is consistent with a predisposition to, or diagnosis of, ABCA4-related conditions.
- ABCA4-related disorders consist of a spectrum of phenotypically overlapping retinal dystrophies (PMID: 26527198, 12789571). CRD is characterized by progressive decreased visual acuity of the central field, photophobia, and poor color vision noted in the first decade of life; night blindness, loss of peripheral vision, and nystagmus also typically occur (PMID: 12037008, 12796258). STGD, also known as fundus flavimaculatus, shows early-stage clinical overlap with CRD, and is characterized by onset of slowly progressive central vision loss in childhood (though first presentation may be in adulthood in STGD); while those affected with STGD do experience night blindness, they typically retain peripheral vision (PMID: 25444351, 21510770). RP initially presents differently from CRD, though they both eventually result in similar clinical phenotypes (PMID: 17270046, 10874631). RP first presents with night blindness and loss of peripheral vision; affected individuals eventually lose central vision (PMID: 26835369, 10874631). RP is highly variable in regards to severity, clinical symptoms, and age of onset (PMID: 17296890).
- Testing parents or additional informative relatives could assist in determining phase, contributing evidence to allow variant reclassification or informing recurrence risk. Please contact Invitae Client Services with any follow-up questions.

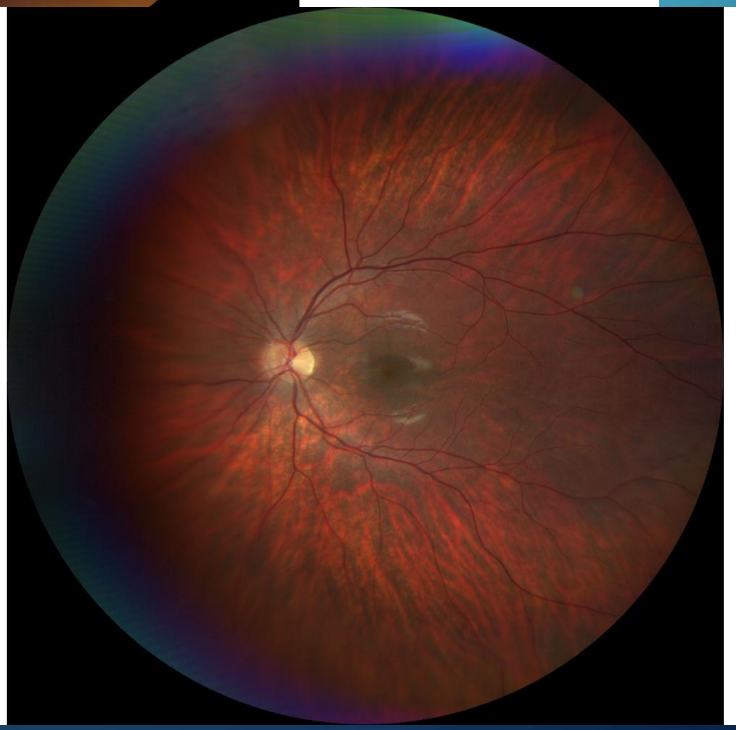
ADDITIONAL CASES

VISION LOSS

- 9 year old male, high myope presents with decreased vision for ERG
- 20/50 OD, 20/80 OS

- Very high myope (about -7 OD, OS)

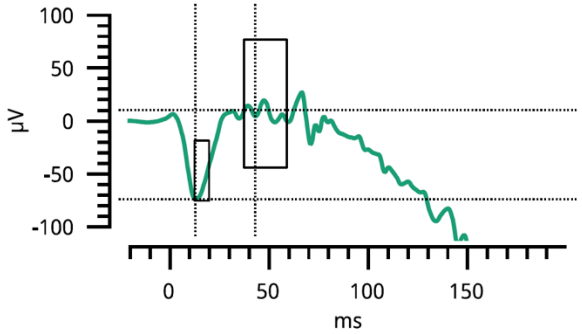




Test #2: Flash: 3.0 cd·s/m², Chromaticity (0.33, 0.33) at 0.1 Hz Background: 0.0 cd/m²

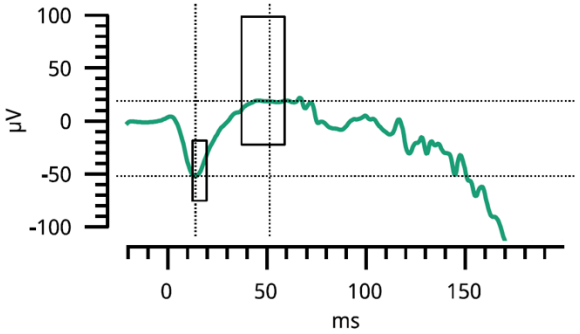
Right Eye (Pupil 9.1 mm)

a-wave		b-wave	
ms	µV	ms	µV
12.4 ↔ 19.7	-18.5 ↔ -75.5	37.3 ↔ 59.0	29.6 ↔ 151
12.9 (6%)	-73.9 (100%)	42.9 (32%)	84.5 (80%)



Left Eye (Pupil 8.0 mm)

a-wave		b-wave	
ms	µV	ms	µV
12.4 ↔ 19.7	-18.5 ↔ -75.5	37.3 ↔ 59.0	29.6 ↔ 151
14.1 (34%)	-52.2 (91%)	51.4 (85%)	71.0 (56%)



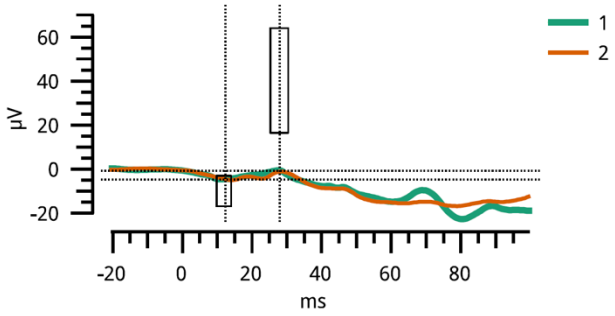
Start: 10:39 AM, Duration: 0 hour(s) 0 min(s)
Background: 30 cd/m², Chromaticity (0.33, 0.33)

Start: 10:41 AM, Duration: 0 hour(s) 0 min(s)
Background: 30 cd/m², Chromaticity (0.33, 0.33)

Test #5: Flash: 3.0 cd·s/m², Chromaticity (0.33, 0.33) at 2 Hz Background: 30 cd/m², Chromaticity (0.33, 0.33)

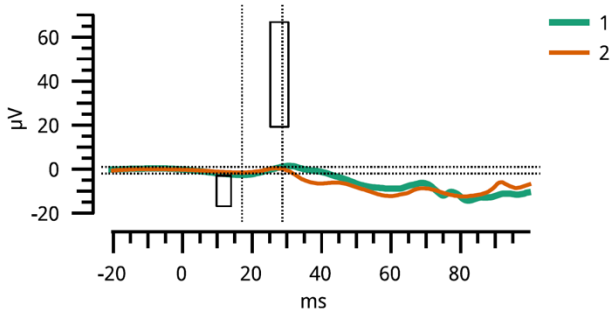
Right Eye (Pupil 3.2 mm)

	a-wave		b-wave	
	ms	µV	ms	µV
	9.8 ↔ 14.0	-3.0 ↔ -16.9	25.2 ↔ 30.4	21.2 ↔ 68.8
1	10.6 (13%)	-4.6 (7%)	27.5 (45%)	4.1 (0%)
2	14.1 (100%)	-5.0 (10%)	28.4 (77%)	3.9 (0%)
	12.4 (68%)	-4.8 (9%)	28.0 (64%)	4.0 (0%)



Left Eye (Pupil 8.2 mm)

	a-wave		b-wave	
	ms	µV	ms	µV
	9.8 ↔ 14.0	-3.0 ↔ -16.9	25.2 ↔ 30.4	21.2 ↔ 68.8
1	17.3 (100%)	-2.6 (0%)	30.6 (100%)	4.1 (0%)
2	16.9 (100%)	-1.5 (0%)	26.9 (27%)	1.9 (0%)
	17.1 (100%)	-2.1 (0%)	28.7 (83%)	3.0 (0%)



FOUND: RP1L1

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is heterozygous for *RP1L1* c.251C>T, p.(Pro84Leu), which is a variant of uncertain significance (VUS).

ADDITIONAL FINDINGS

The patient is heterozygous for *ABCA4* c.733T>C, p.(Tyr245His), which is a variant of uncertain significance (VUS).

Please see APPENDIX 2: Additional Findings for further details

RP1L1 c.251C>T, p.(Pro84Leu)

There are 2 individuals heterozygous for this variant in gnomAD, a large reference population database (n>120,000 exomes and >15,000 genomes) which aims to exclude individuals with severe pediatric disease. All in silico tools utilized predict that this variant will be damaging to protein structure and function. The affected amino acid is highly conserved in mammals as well as in evolutionarily more distant species, which suggests that this position does not tolerate variation. There is a moderate physicochemical difference between proline (Pro) and leucine (Leu), therefore this is considered a non-conservative substitution (Grantham score = 98 [0-215]). To the best of our knowledge, this variant has not been described in the medical literature or reported in disease-related variation databases such as ClinVar or HGMD. We have previously reported this variant as heterozygous in a patient with pattern dystrophy (BpG unpublished observations).

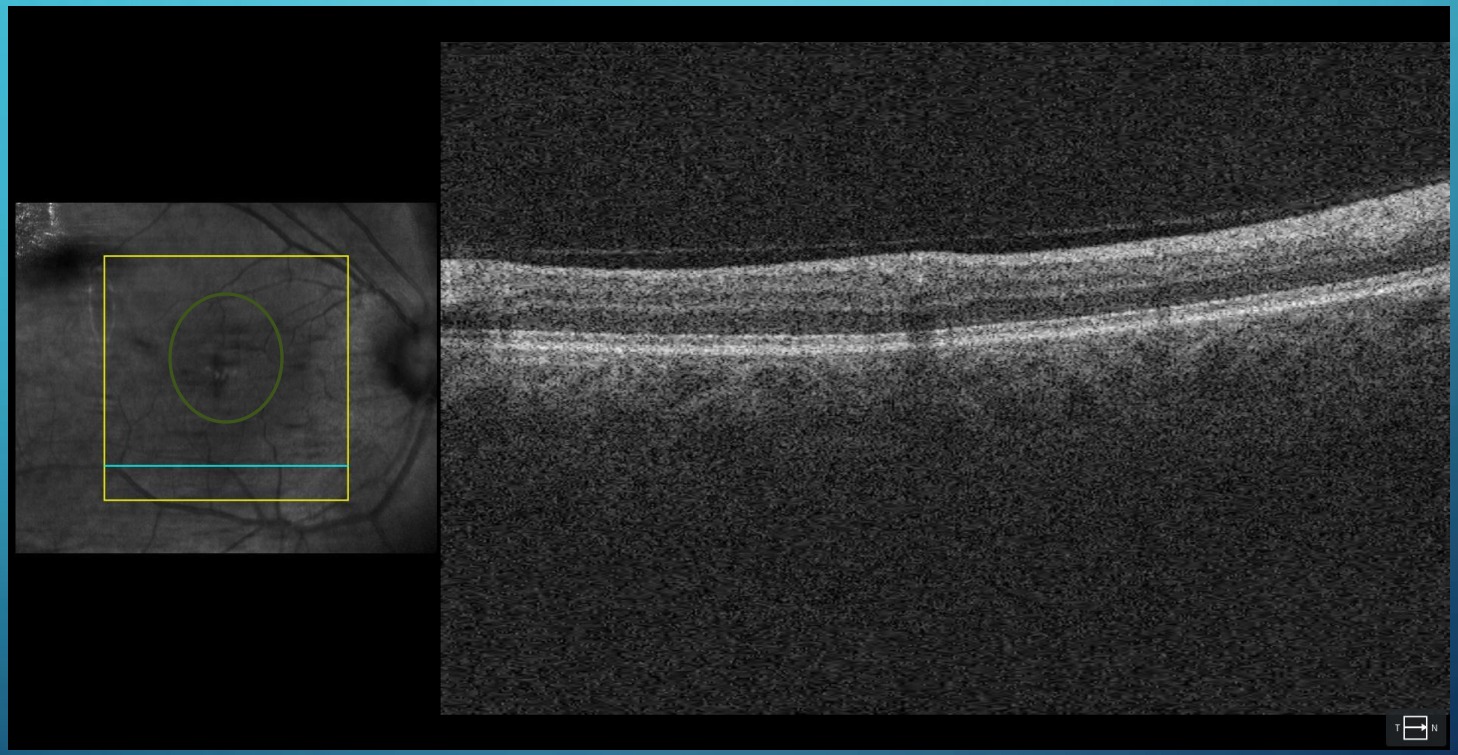
RP1L1

RP1L1 (MIM*608581) encodes a protein that shares 35% amino acid identity with *RP1*, a gene responsible for 5 to 10% of cases with autosomal dominant retinitis pigmentosa. Variants in *RP1L1* have been associated with autosomal dominant occult macular dystrophy (OCMD; MIM#613587) and autosomal recessive retinitis pigmentosa (arRP; MIM #618826). *RP1L1*-associated photoreceptor disease has been recently summarized by Noel et al (PMID: 32360662). OCMD is an autosomal-dominant form of inherited macular dystrophy characterized by a progressive decrease of visual acuity due to macular dysfunction (PMID: 2774037, 8909203). The disorder was termed "occult" because the macular dysfunction of this disease is hidden by a normal fundus appearance. Typical OCMD, as described by Miyake *et al.* (PMID: 25665791), is characterized by central cone dysfunction and occasionally rod dysfunction, leading to a loss of vision despite normal ophthalmoscopic appearance, normal fluorescein angiography, and normal full-field electroretinograms (ERGs). Abnormal focal macular ERGs and blurring of the IS/OS junction and the disappearance of the cone outer segment tip (COST) line in SD-OCT images have been reported (PMID: 22605915). OCMD has a broad range of age at onset (6 to 81 years). Thirty distinct variants [23 disease-causing (DM) and 7 likely disease-causing (DM?)] have been associated with OCMD according to HGMD® Professional 2022.2; all but three of these are missense, one is a nonsense, one is a frameshift and one is a small indel variant (Sui *et al.* ARVO Annual Meeting Abstract, June 2017, PMID: 27623337).

Homozygous variants in *RP1L1* have recently been reported in patients with autosomal recessive retinitis pigmentosa. Two homozygous truncating variants and one homozygous missense variant [c.601delG, p.(Lys203Argfs*28); c.1972C>T p.(Arg658*); c.1637G>C, p.(Ser546Thr)] have been associated with typical retinitis pigmentosa (PMID: 23281133, 25324289). Also, nonsense variant *RP1L1* c.5959C>T, p.(Gln1987*) has been reported in a patient with RP. The variant presumably was detected in the homozygous state (PMID: 26355662). In addition, a homozygous missense variant, *RP1L1* c.3628T>C p.(Ser1210Pro), has been reported in a patient with cone dystrophy (PMID: 25692141). Recently, Zobor *et al.* described four RP patients with biallelic variants in *RP1L1* (PMID: 30025130). The first patient, diagnosed with RP at age 35, had a homozygous nonsense variant *RP1L1* c.3022C>T, p.(Gln1008*). Two siblings had the *RP1L1* c.5959C>T, p.(Gln1987*) variant together with a missense variant *RP1L1* c.455G>A, p.(Arg152Gln). The fourth patient (arRP4, male, 40 years) had been suffering from night blindness and slowly progressing visual field loss for 10 years, and had a homozygous nonsense variant *RP1L1* c.1107G>A, p.(Trp369*). All arRP cases described by Zobor *et al.* were mild with disease onset ≈30 years and preserved ERG-responses.

RP1L1 variants have historically been associated with occult macular dystrophy and RP; however, there is increasing evidence that *RP1L1* variants may play a role in additional photoreceptor diseases and/or that OCMD may be an early stage of more severe macular degenerations (PMID: 32360662). In a recent review, a patient with severe macular degeneration and compound heterozygous variants in *RP1L1*, c.1370C>G, p.(Ser457Cys) and c.4396G>T, p.(Glu1466*) (both absent in gnomAD), and a mother and daughter with adult pseudovitelliform macular dystrophy, both heterozygous for missense variant, *RP1L1* c.1994C>G, p.(Pro665Arg) (also absent in gnomAD), have been reported (PMID: 32360662).

CASE 5: SURE LOOKS GENETIC TO ME….

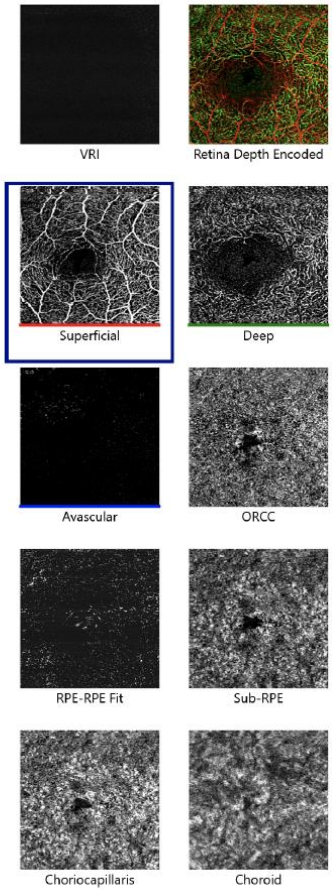


PATIENT PRESENTS

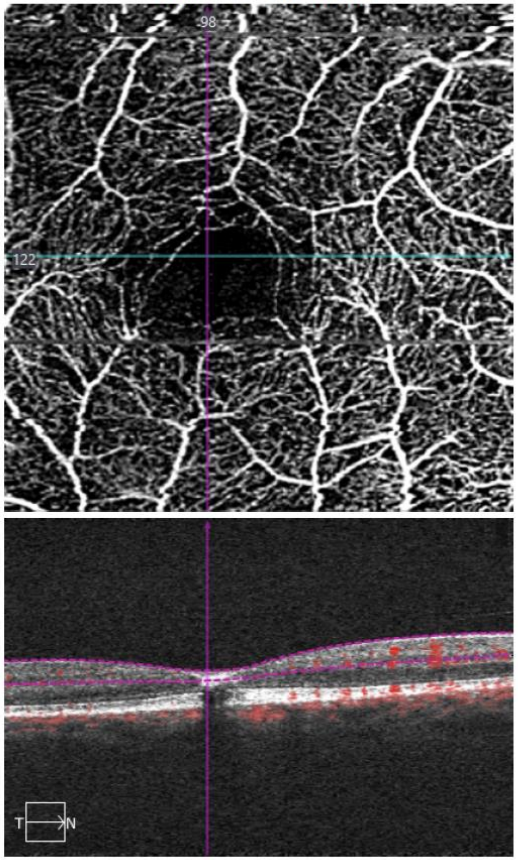
- Patient presents for ERG/EOG for questionable pattern dystrophy
- looks like a pattern dystrophy to me too.
- Symmetrical between eyes and has been there for several years

Angiography Analysis : Angiography 3x3 mm

OD ● | ○ OS

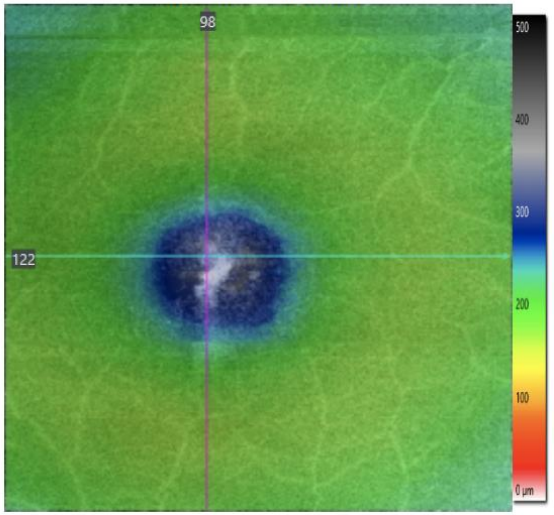


AngioPlex - Superficial



Slice: 122 Top: ILM Bottom: IPL

Structure - Superficial



Overlays
Structure - Thickness Map
AngioPlex - None

Tracked during scan

GENETICS

- Blank. Not helpful in anyway.
- So its not these 314 genes….

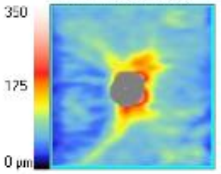
CASE 6: OPTIC NERVE ISSUES

- 18 year old patient referred to neuro-ophthalmology for optic atrophy with possible RP component?

- Vision very poor (20/400 OD, OS) has been since birth.
- Optic atrophy by age 5
- Sister has too
- Considered Lebers (mitochondrial, usually not in this panel).
- Ran genetics due to RP concern around peripheral pigment changes.

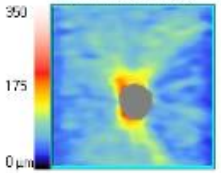
ONH and RNFL OU Analysis:Optic Disc Cube 200x200 OD ● | ● OS

RNFL Thickness Map

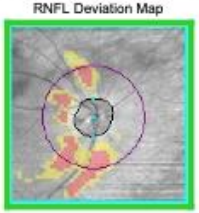


	OD	OS
Average RNFL Thickness	81 µm	75 µm
RNFL Symmetry	72%	
Rim Area	1.35 mm²	1.33 mm²
Disc Area	1.36 mm²	1.33 mm²
Average C/D Ratio	0.08	0.08
Vertical C/D Ratio	0.07	0.07
Cup Volume	0.000 mm³	0.000 mm³

RNFL Thickness Map

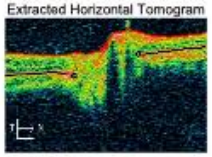


RNFL Deviation Map

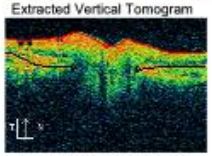


Disc Center(-0.21,-0.06)mm

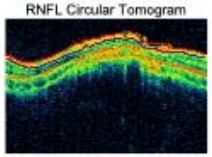
Extracted Horizontal Tomogram



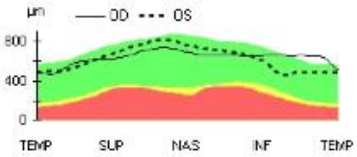
Extracted Vertical Tomogram



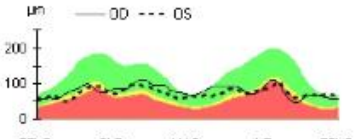
RNFL Circular Tomogram

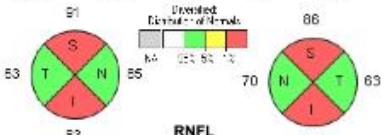


Neuro-retinal Rim Thickness



RNFL Thickness



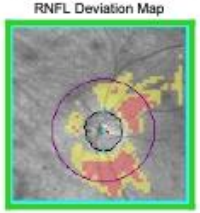


RNFL Quadrants

RNFL ClockHours

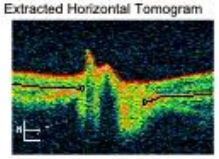
RNFL Thickness Map

RNFL Deviation Map

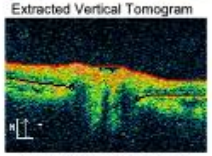


Disc Center(0.09,-0.51)mm

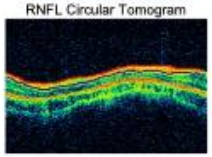
Extracted Horizontal Tomogram



Extracted Vertical Tomogram

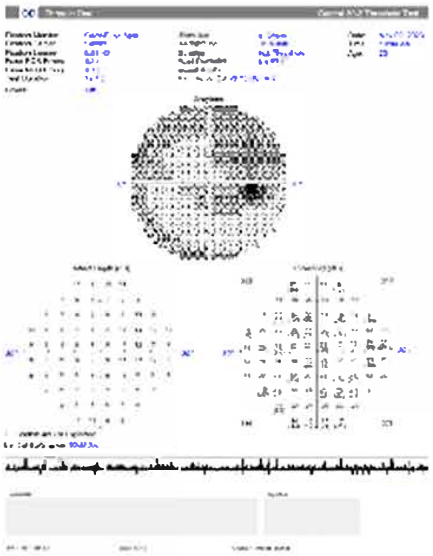


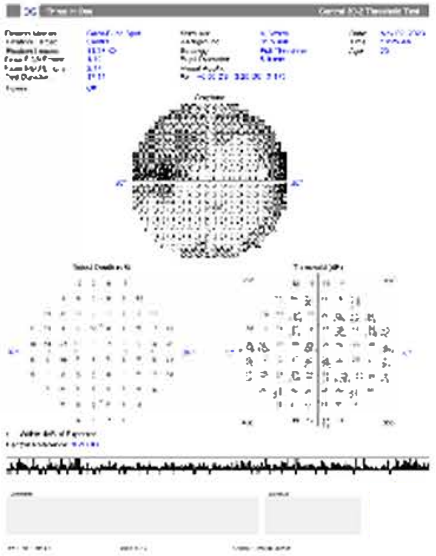
RNFL Circular Tomogram



Comments

Doctor's Signature





GENE FOUND

- Gene is for optic atrophy.
- No RP component
- Gives clear picture

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is heterozygous for *ACO2* c.487G>T, p.(Val163Leu), which is a variant of uncertain significance (VUS).
The patient is heterozygous for *ACO2* c.1894G>A, p.(Val632Met), which is a variant of uncertain significance (VUS).

ADDITIONAL FINDINGS

The patient is heterozygous for *PPT1* c.329A>G, p.(Asn110Ser), which is a variant of uncertain significance (VUS).
The patient is heterozygous for *CERKL* c.908A>G, p.(Asn303Ser), which is a variant of uncertain significance (VUS).
The patient is heterozygous for *LCA5* c.511C>T, p.(Leu171Phe), which is a variant of uncertain significance (VUS).

Please see APPENDIX 2: Additional Findings for further details

OPTIC ATROPHY GENE

ACO2 c.487G>T, p.(Val163Leu)

There are 31 individuals heterozygous for this variant in gnomAD v2, a large reference population database (n>120,000 exomes and >15,000 genomes) which aims to exclude individuals with severe pediatric disease. The variant is predicted to be tolerated by most *in silico* tools utilized. The variant has previously been seen in a compound heterozygous state with a variant of uncertain significance *ACO2* c.1894G>A, p.(Val632Met) in two siblings with optic atrophy. Their mother, who was not reported to be affected, was not a carrier of the *ACO2* c.487G>T, p.(Val163Leu) variant, while the father was not available for testing (PMID: 32449285). We have detected the *ACO2* c.487G>T, p.(Val163Leu) variant as heterozygous in several individuals with other underlying pathogenic genetic variants that better explain their eye findings (BpG, unpublished observation). The variant has been submitted to ClinVar by other clinical testing laboratories (variation ID 214016).

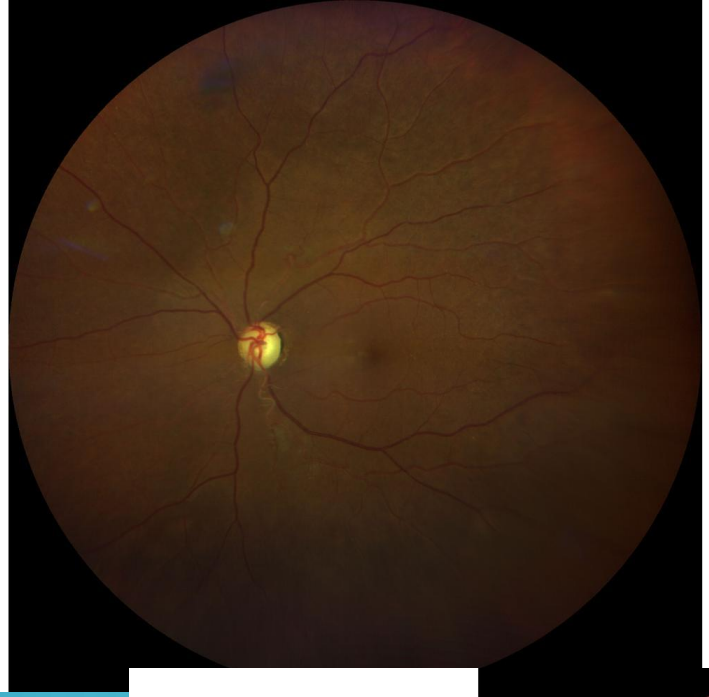
***ACO2* c.1894G>A, p.(Val632Met)**

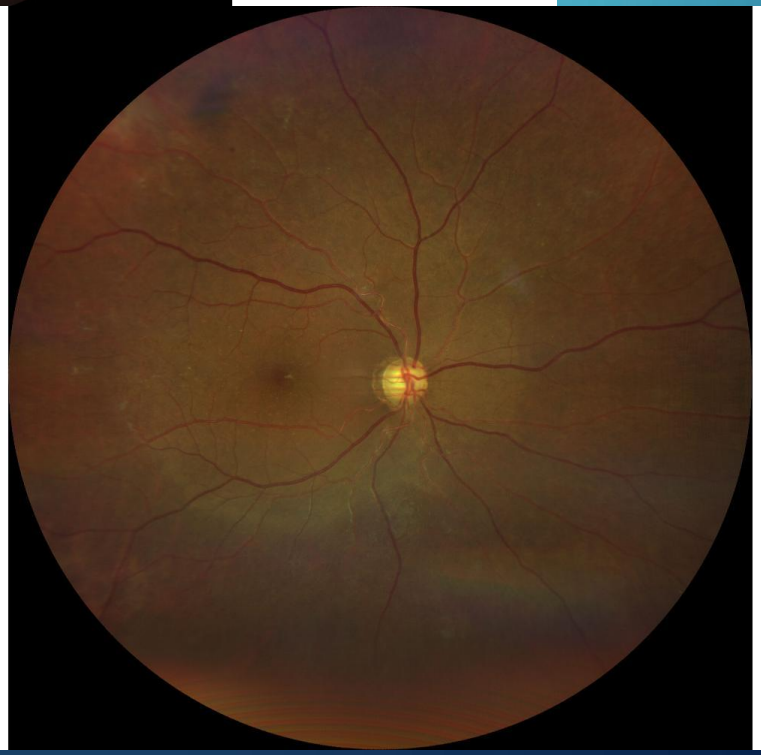
This variant is absent in gnomAD v2, a large reference population database (n>120,000 exomes and >15,000 genomes) which aims to exclude individuals with severe pediatric disease. The variant is predicted to be deleterious by all in silico tools utilized. This variant has been reported in the literature as compound heterozygous with variant of uncertain significance *ACO2* c.487G>T, p. (Val163Leu) in two siblings with optic atrophy (PMID: 32449285). Their mother, who was not reported to be affected, was a carrier of the *ACO2* c.1894G>A, p.(Val632Met) variant. The father was unavailable for testing. The variant has been submitted to ClinVar by other clinical testing laboratories (variation ID: 830372).

ACO2

CASE 7: ANOTHER DOCTOR ASKS FOR HELP

- Patient presents with early onset diabetes and vision loss.
- Patient 20 year old female
- Dr thinks patient may have Wolfram syndrome based on clinical history.
- At the time the gene for Wolfram was in the panel so it was collected






OD
Central 30-2 Threshold Test
Structure-Function OU (Single Exam)
Central 30-2 Threshold Test
OS
Graytone
Total Deviation
Pattern Deviation
MD Threshold exceeded.
See Total Deviation plot.
Consider 10-2 testing.
P < 5%
P < 2%
P < 1%
P < 0.5%
Graytone
Total Deviation
Pattern Deviation
MD Threshold exceeded.
See Total Deviation plot.
Consider 10-2 testing.
Sep 23, 2024 SITA-Standard
FP: 38% XX
FN: N/A
FL: 8/17 XX
VFI24-2: 16%
MD30-2: -28.00 dB P < 0.5%
PSD30-2: 8.96 dB P < 0.5%
GHT: Outside Normal Limits
RNFL Thickness
OD
OS
TEMP
SUP
NAS
INF
TEMP
Sep 23, 2024 SITA-Standard
FP: 18% XX
FN: 71%
FL: 8/17 XX
VFI24-2: 20%
MD30-2: -26.21 dB P < 0.5%
PSD30-2: 8.37 dB P < 0.5%
GHT: Outside Normal Limits
OD
CIRRUS HD-OCT
RNFL Thickness Map
Signal Strength: 7/10
RNFL Quadrants
RNFL Clock Hours
Signal Strength: 8/10
RNFL
Jun 12, 2024
Ganglion Cell
Jun 12, 2024
CIRRUS HD-OCT
OS
RNFL Quadrants
RNFL Clock Hours
RNFL Thickness Map
Signal Strength: 4/10
RNFL
Jun 12, 2024
OD
OS
51µm
Average RNFL Thickness
45µm
0.78
Average C/D Ratio
0.78
0.79mm²
Rim Area
0.77mm²
0.78
Vertical C/D Ratio
0.74
0.368mm³
Cup Volume
0.380mm³
1.87mm²
Disc Area
2.10mm²
48µm
Average GCL + IPL Thickness
X
39µm
Minimum GCL + IPL Thickness
X
Distribution of Normals
NA
99%
5%
1%
At least one parameter is close to a normative limit that may change the color coding on a re-scan.
Comments
Signature
Version 3.5.1.0
Created: Sep 23, 2024 10:53:20 AM

WOLFRAM SYNDROME

- diabetes and vision loss before 15
- Has some trials and possible treatments available

1. **Diabetes mellitus (age 6):** Diabetes mellitus is a problem with your body's ability to absorb sugar (glucose) from the food you eat. Normally, your pancreas makes insulin, which helps your cells absorb sugars (glucose) from your bloodstream. If you don't make enough insulin or if your cells don't respond to insulin, your blood sugar can rise too high. Wolfram syndrome-related diabetes is similar to Type 1 diabetes, but it's not an autoimmune disease. Diabetes symptoms include frequent urination, increased thirst, blurred vision and unexplained weight loss.
2. **Optic atrophy (age 11):** Optic atrophy is the degeneration of your optic nerve, which carries signals from your eyes to your brain. Symptoms include blurred, dulled or reduced peripheral (side) vision.
3. **Sensorineural hearing loss (age 13):** Sensorineural hearing loss occurs due to damage in your inner ear. This type of hearing loss usually gets worse as you get older and can lead to deafness.
4. **Diabetes insipidus (age 14):** Diabetes insipidus isn't related to diabetes mellitus. It's an issue with the production of an antidiuretic hormone that controls the amount of water in your urine (pee). People with diabetes insipidus have large amounts of watery urine. This excess urination can cause dehydration, electrolyte disturbance, weakness, dry mouth and constipation.

- :Cleveland clinic

GENES BACK!

- Patient does have wolfram gene!!
- Helps with improved treatment for her an her family!

CONCLUSION

- Genetics can sometimes be helpful in better understanding what is going on with a patient.
- They do not always provide the information wanted however
- They will likely increase over the coming years.