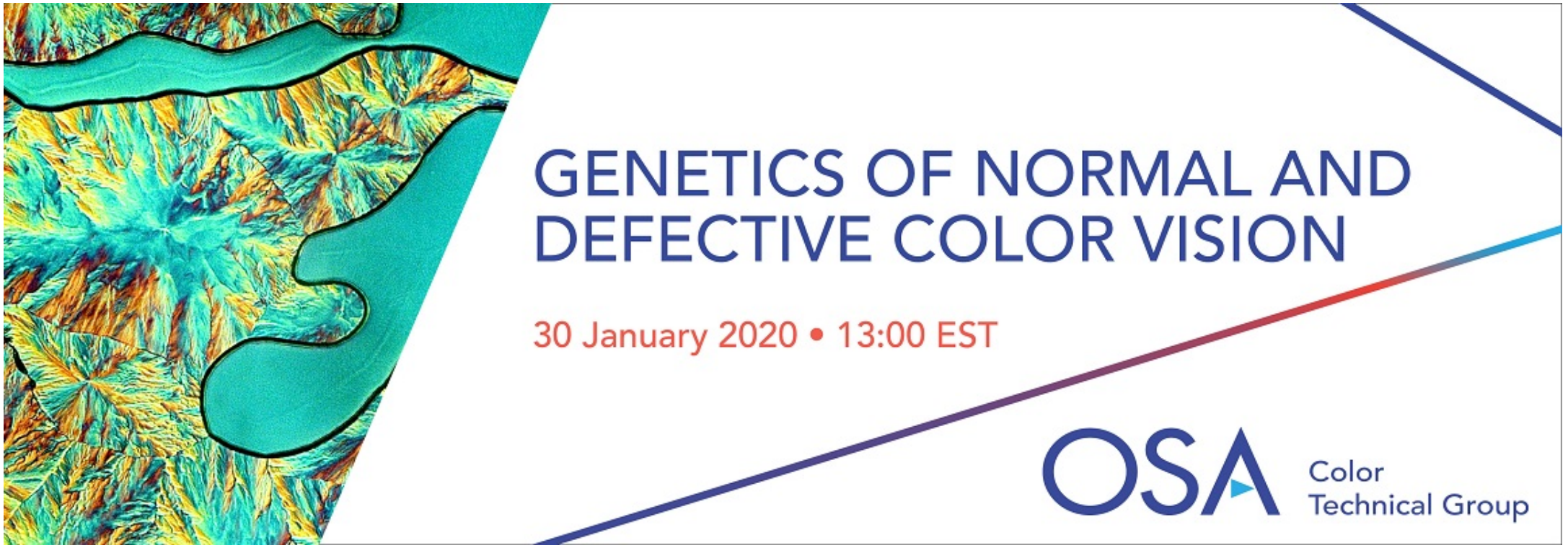
Genetics of Normal and Defective Color Vision

Presented by:

OSA Color Technical Group

The **OSA Color Technical Group** welcomes you!



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Our Technical Group at a Glance

Our Focus

- “all aspects related to the physics, physiology, and psychology of color in biological and machine vision”

Our Mission

- To benefit *YOU*
- Webinars, social media, publications, technical events, outreach
- Interested in presenting your research? Have ideas for TG events? Contact Manuel Spitschan (Chair) at manuel.spitschan@psy.ox.ac.uk

Where To Find Us

- Website: https://www.osa.org/en-us/get_involved/technical_groups/vc/color_(vc)/
- Twitter: #OSAColorTG
- LinkedIn: https://www.linkedin.com/groups/13573604

Save the date!

Speaker: Prof. **Christian Cajochen, UoB, Basel (CH)**

Host: Manuel Spitschan

Today's Webinar

Genetics of Normal and defective color vision.

Prof. Maureen Neitz

Ray H Hill endowed Professor, University of Washington

Speaker's Short Bio:

- Professor in Ophthalmology
- Co-lead of the Neitz Vision Laboratory
- ICVS, Directors Committee

Genetics of Normal and Defective Color Vision

MAUREEN NEITZ, PHD

RAY H. HILL PROFESSOR

VISION SCIENCE CENTER

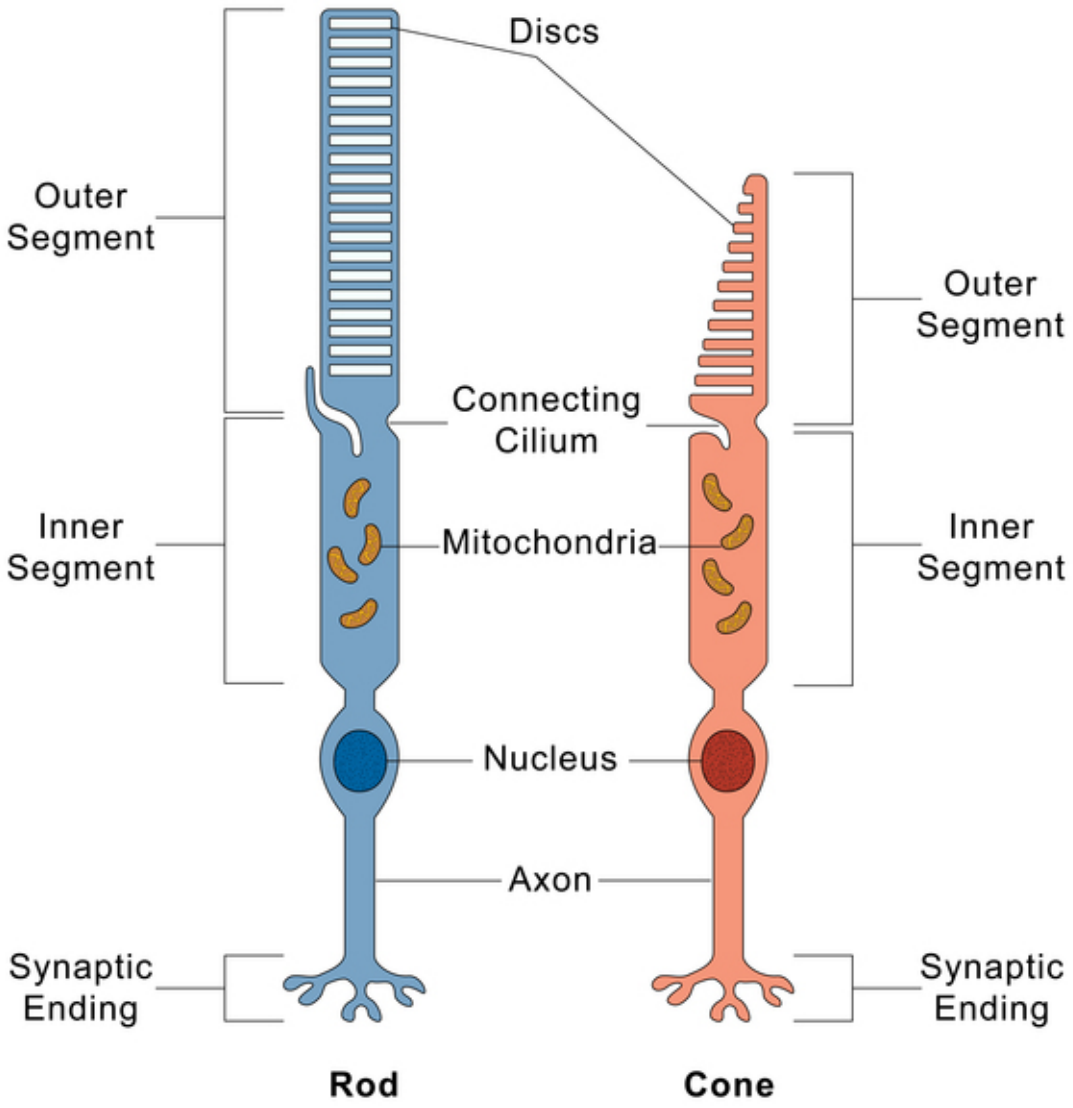
UNIVERSITY OF WASHINGTON

CONES

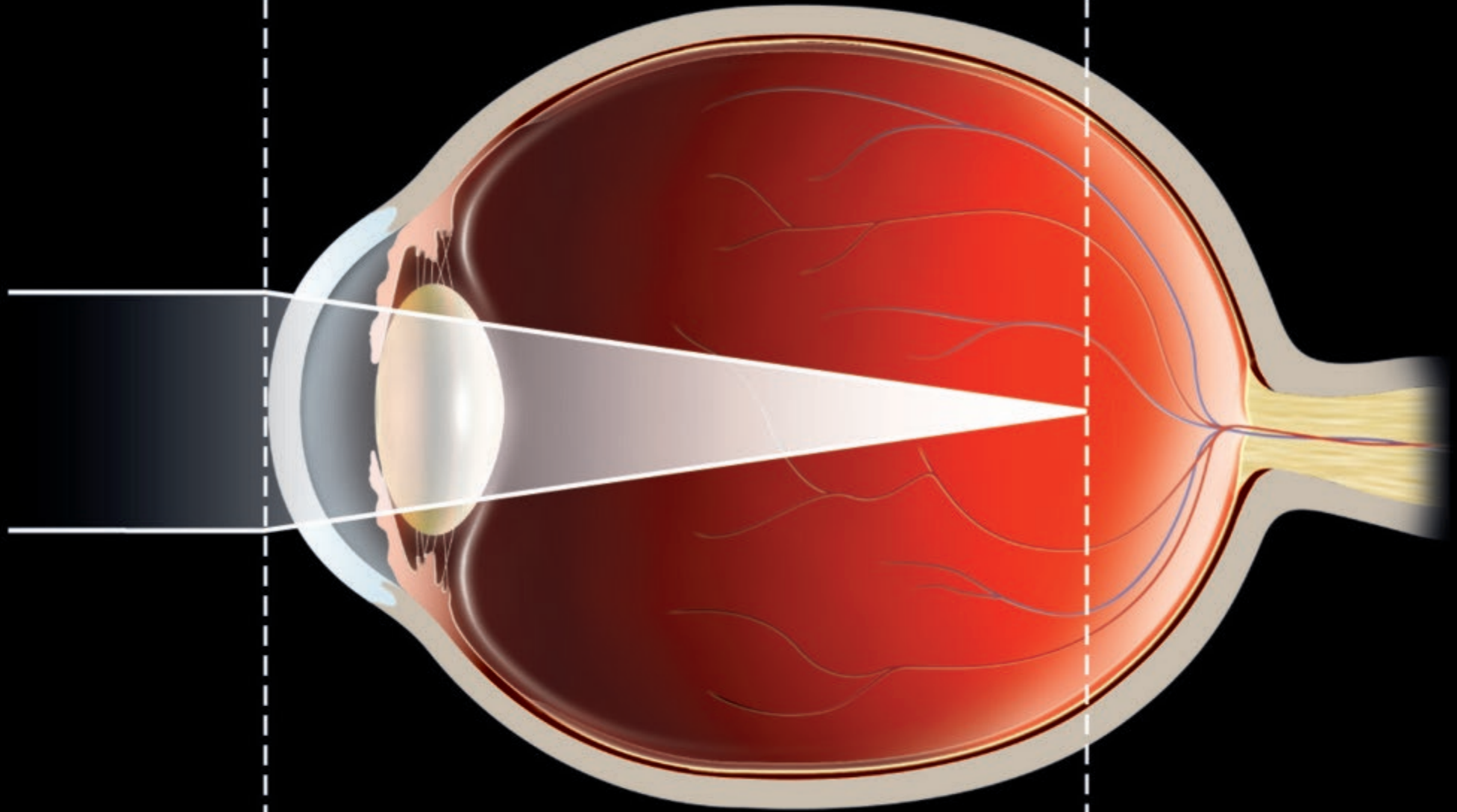
COLOR VISION

HIGH ACUITY VISION

REGULATE EYE GROWTH



Myopia (near sightedness)



Normal Color Vision

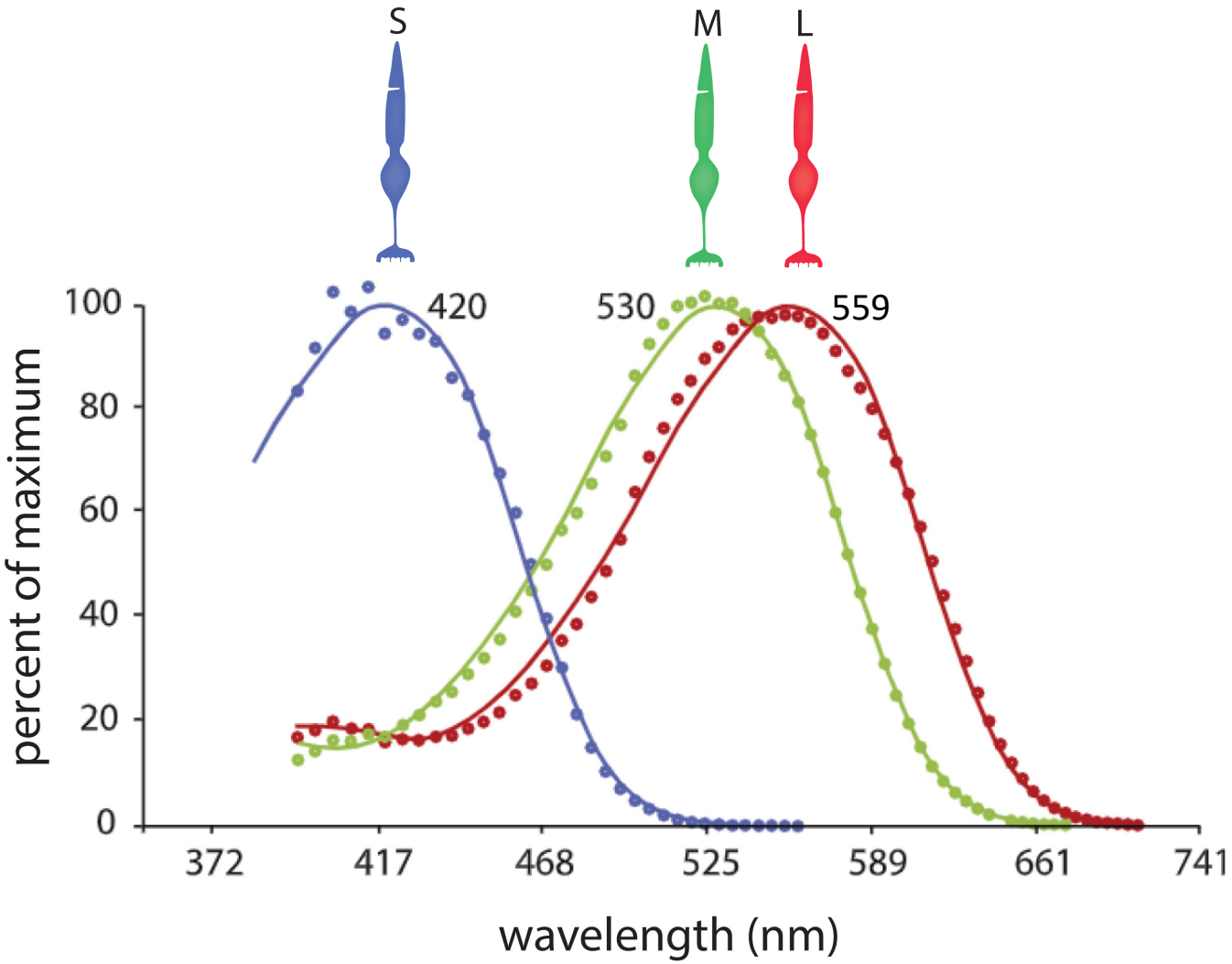
THREE TYPES OF CONE PHOTORECEPTORS

CLASSED ACCORDING TO SPECTRAL SENSITIVITY

L (Long wavelength sensitive) = RED

M (Middle wavelength sensitive) = GREEN

S (Short wavelength sensitive) = BLUE



INHERITED COLOR VISION DEFICIENCIES

HAVE UNUSUAL NAMES THAT DERIVE FROM THE GREEK ROOTS

PROT = 1ST TYPE = red-green color vision defect, no L cone function

DEUT = 2ND TYPE = red-green color vision defect, no M cone function

TRIT = 3RD TYPE = blue-yellow color vision defect, no or reduced S cone function

INHERITED COLOR VISION DEFICIENCIES

Red-green color vision deficiencies affect

1 in 12 males

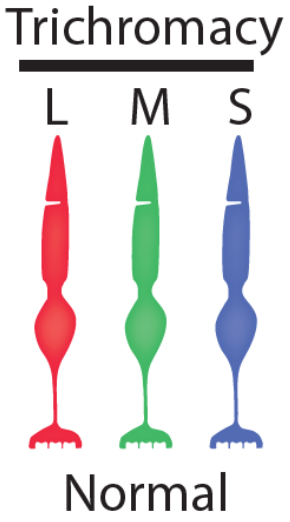
1 in 230 females

Blue-yellow color vision deficiencies affect

very rare, affects males and females equally

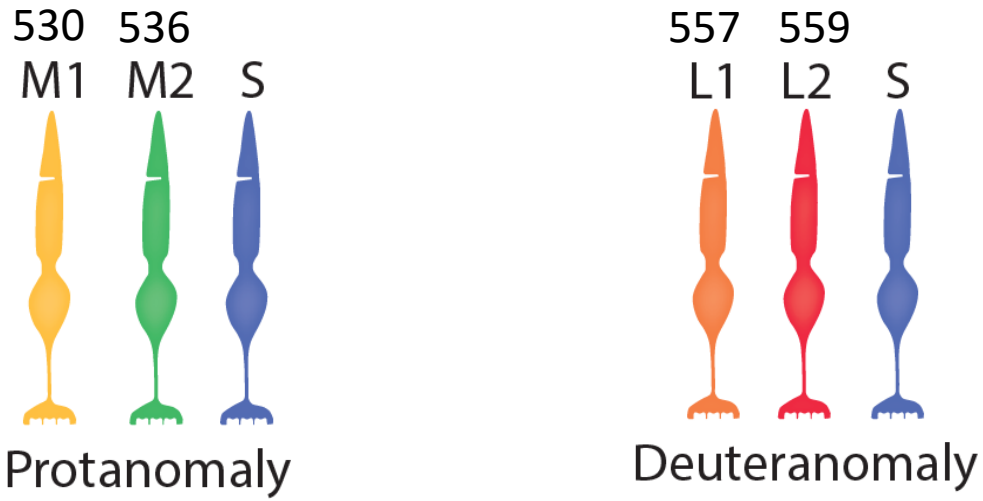
INHERITED COLOR VISION DEFICIENCIES

CATEGORIZED ACCORDING TO THE NUMBER OFFUNCTIONAL CONE TYPES IN THE RETINA



INHERITED COLOR VISION DEFICIENCIES

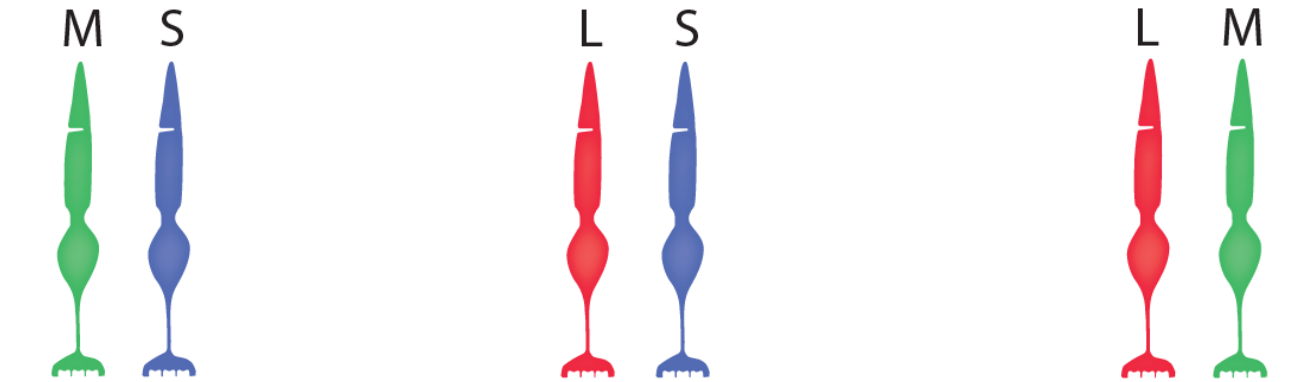
CATEGORIZED ACCORDING TO THE NUMBER OF FUNCTIONAL CONE TYPES IN THE RETINA



ANOMALOUS TRICHROMACIES

INHERITED COLOR VISION DEFICIENCIES

CATEGORIZED ACCORDING TO THE NUMBER OF FUNCTIONAL CONE TYPES IN THE RETINA



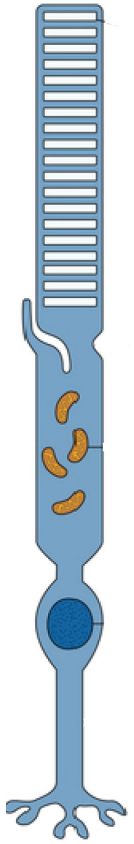
DICHROMACIES

INHERITED COLOR VISION DEFICIENCIES

CATEGORIZED ACCORDING TO THE NUMBER OF FUNCTIONAL CONE TYPES IN THE RETINA

Blue Cone Monochromacy

Rod Monochromacy = Achromatopsia

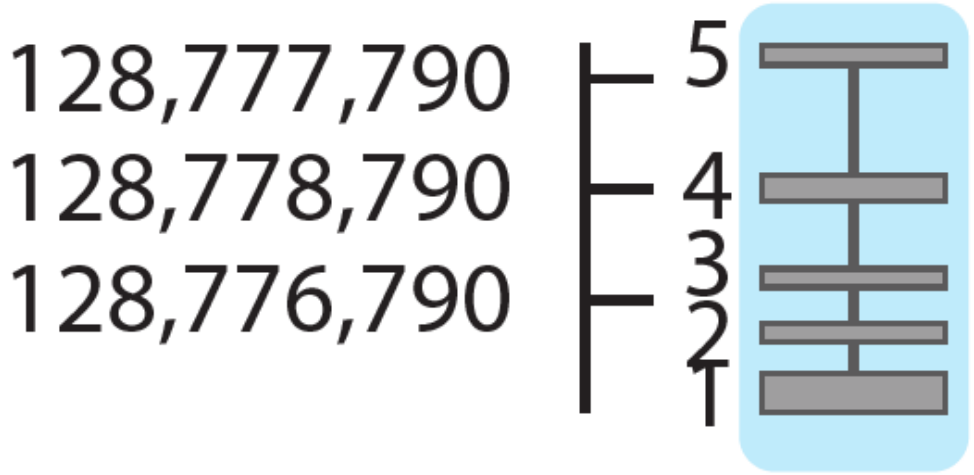


Vision is mediated by rods only

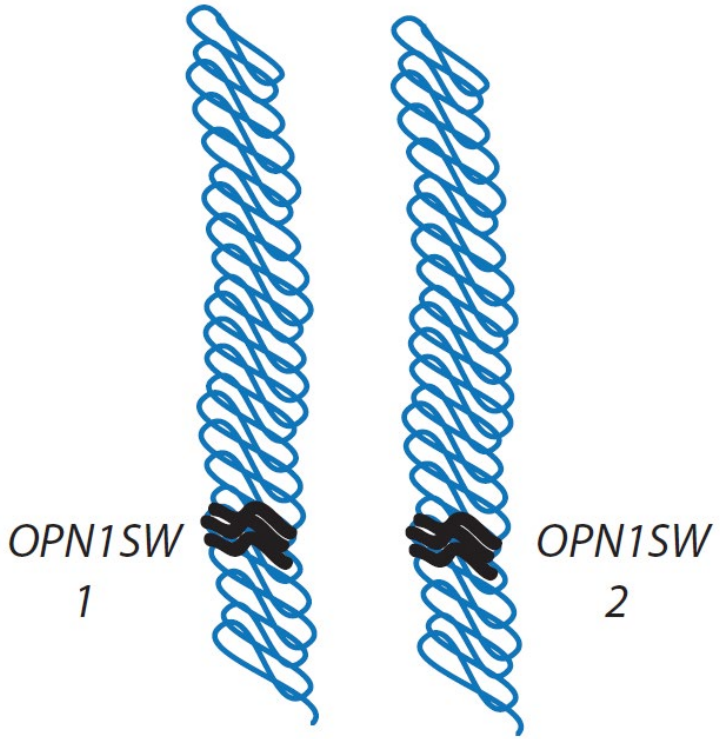
Condition is caused by mutations in at least 6 different genes that are expressed in all 3 cone types, hence lack of all cone contribution to vision.

Estimated to affect 1 in 50,000 to 100,000

OPN1SW



(7q32.1)



Chromosome 7

50% *OPN1SW 1*
50% *OPN1SW 2*

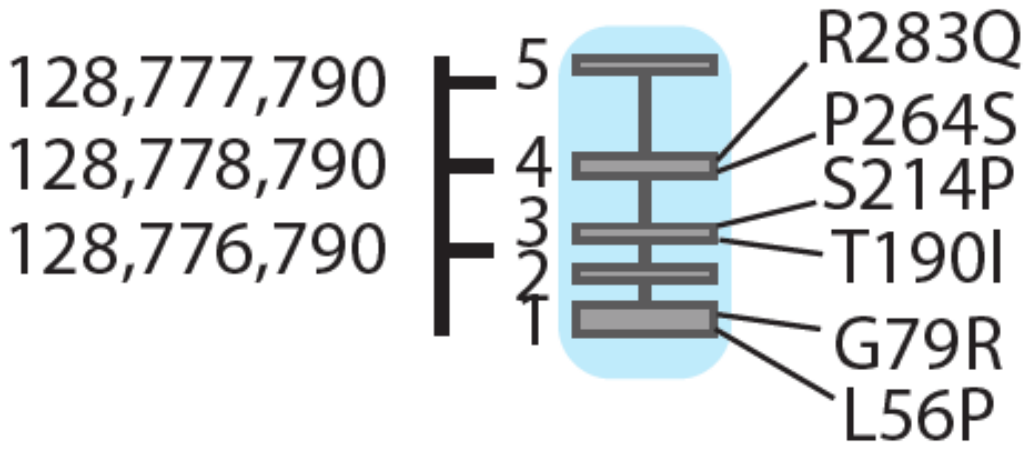
Inherited Tritan Color Vision Defects

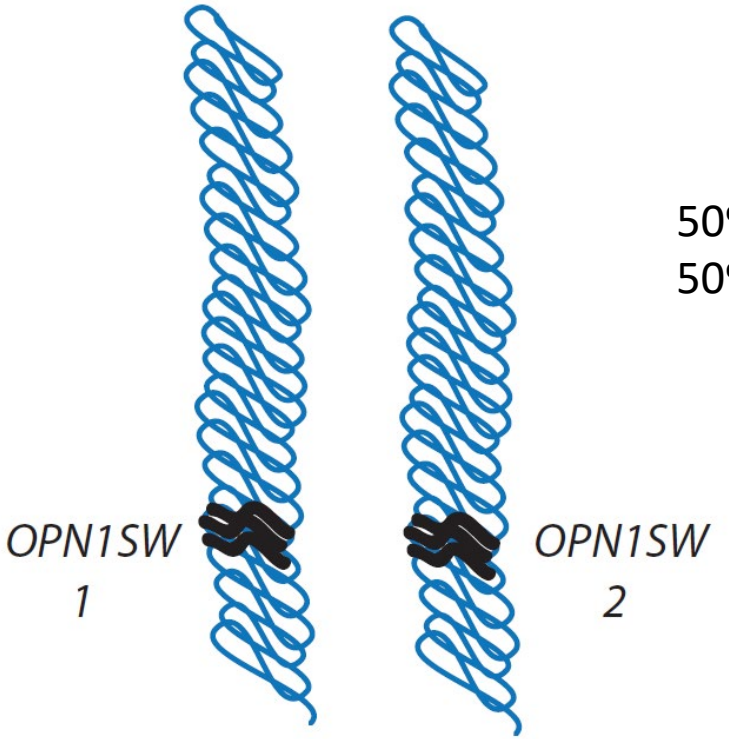
- Autosomal dominant
- Not necessarily congenital

OPN1SW (7q32.1)

- There are the 6 different amino acid substitutions known to cause Tritanopia

- We recently identified a splice site mutation that is associated with loss in blue-yellow color vision, but it is much milder than the tritanopia associated with these amino acid substitutions.



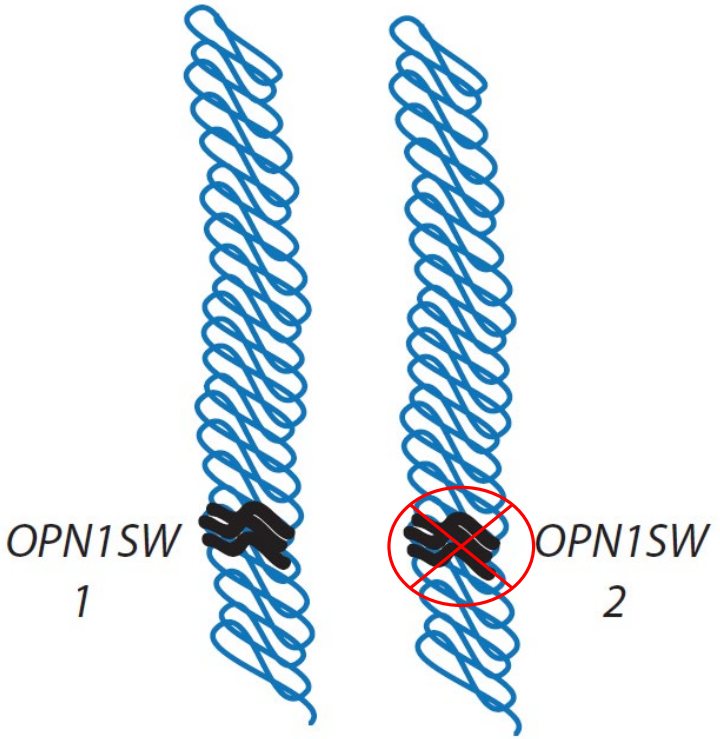


Chromosome 7

50% *OPN1SW 1 (normal)*
50% *OPN1SW 2 (mutant protein)*

Inherited Tritan Color Vision Defects

- Expressing the mutant protein ultimately leads to cone death

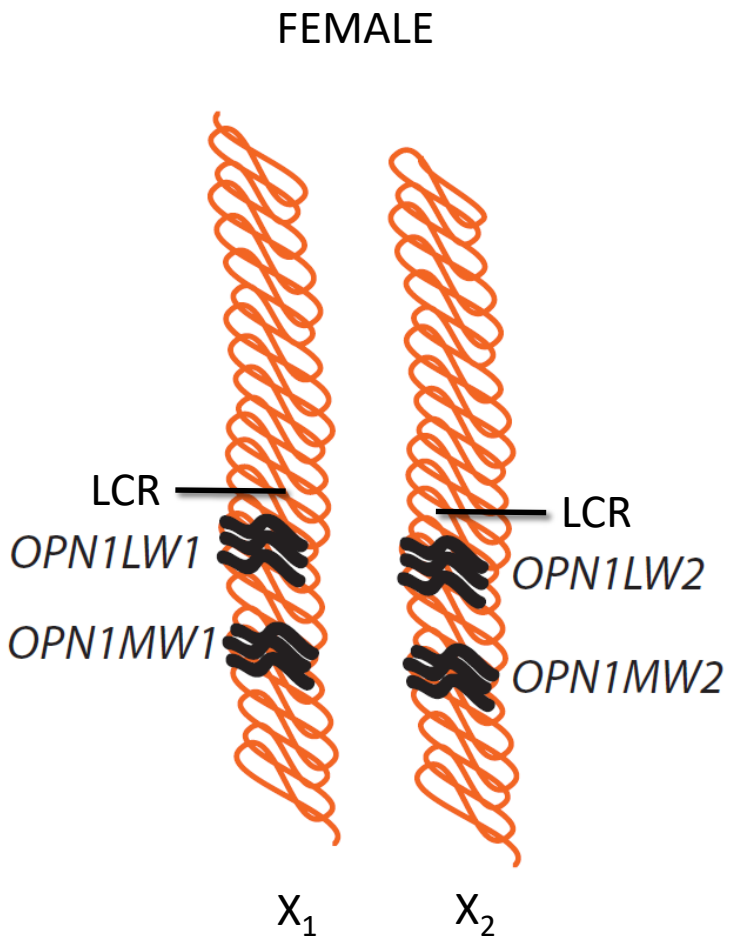


Chromosome 7

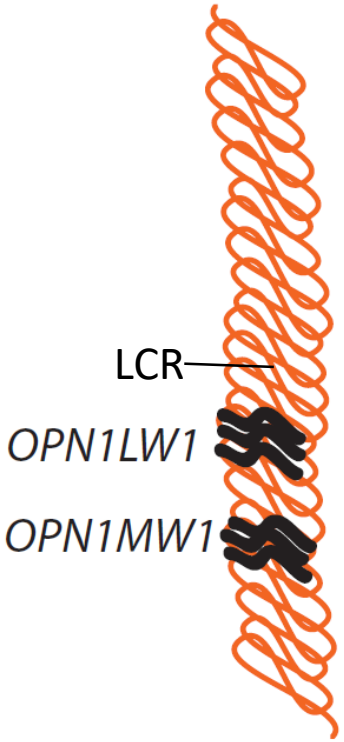
50% *OPN1SW 1*

~~50% *OPN1SW 2*~~

Half the normal amount of photopigment


FEMALE
LCR
OPN1LW1
OPN1MW1
LCR
OPN1LW2
OPN1MW2
X1
X2

MALE



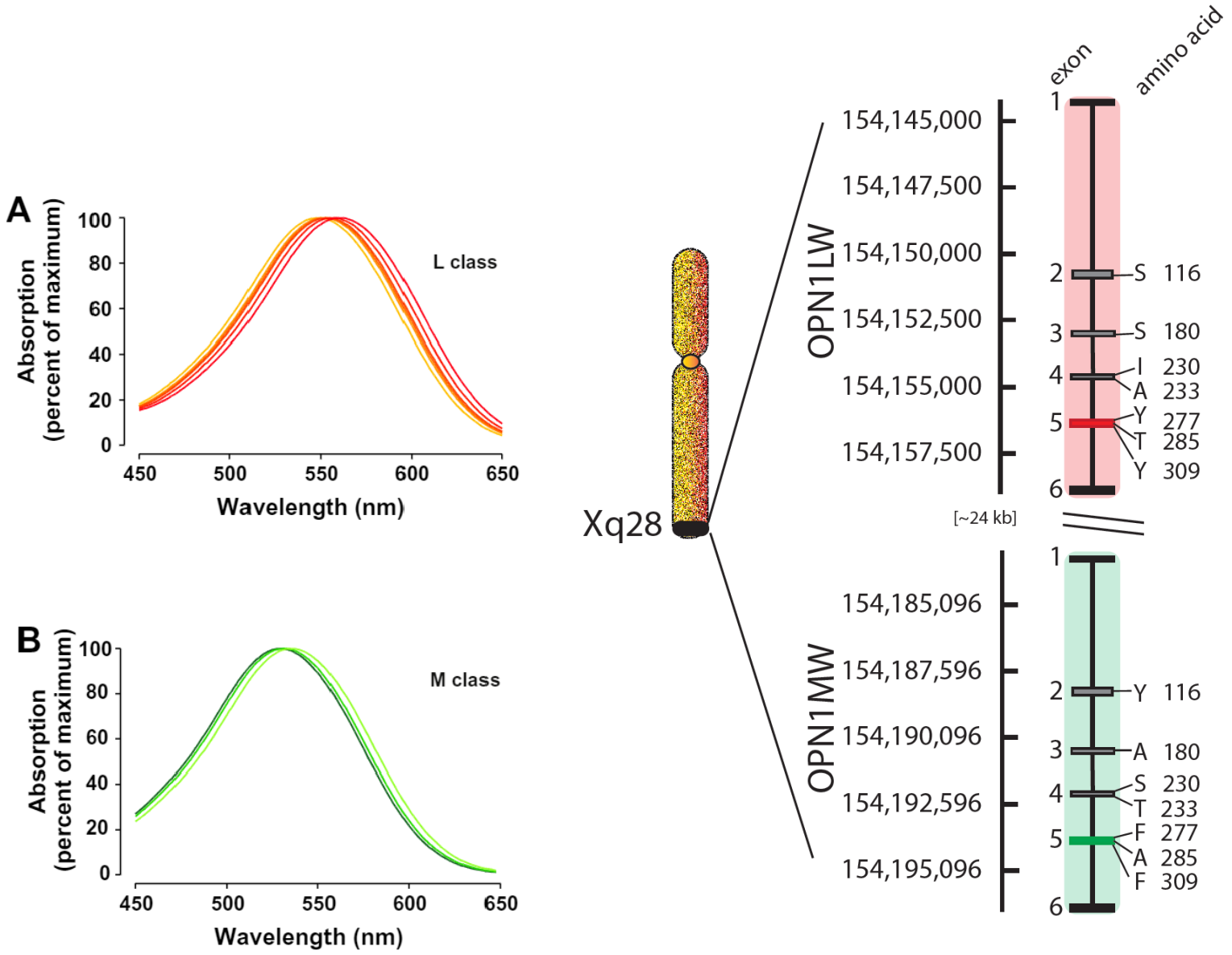
X_1

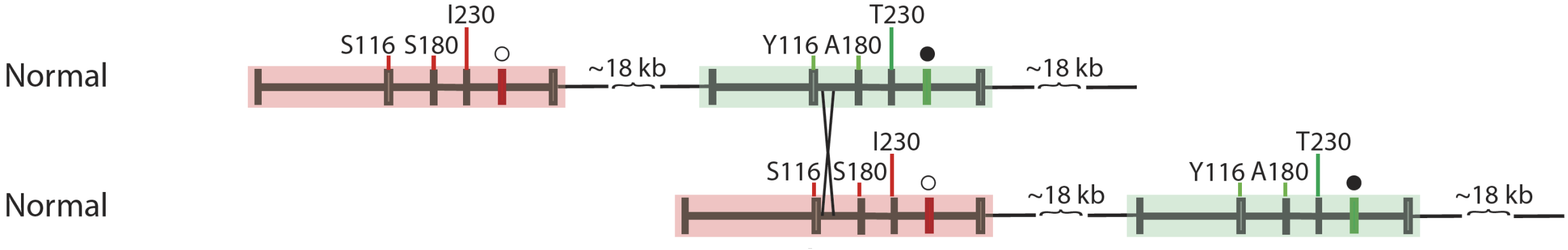
100% *OPN1LW 1*

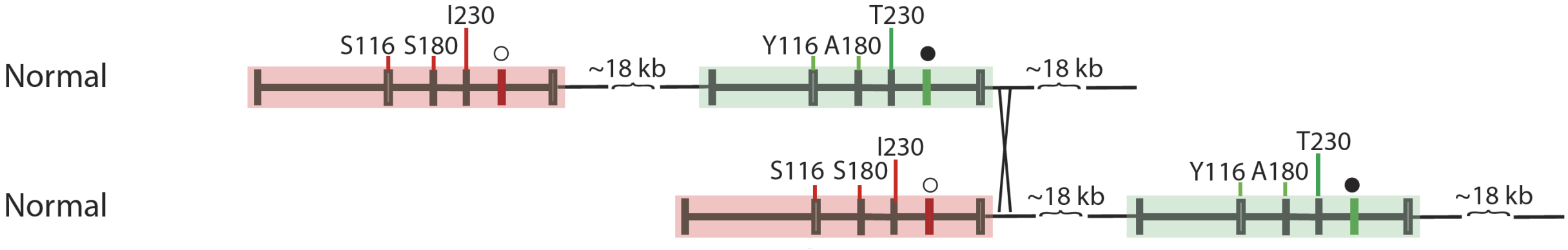
100% *OPN1MW 1*

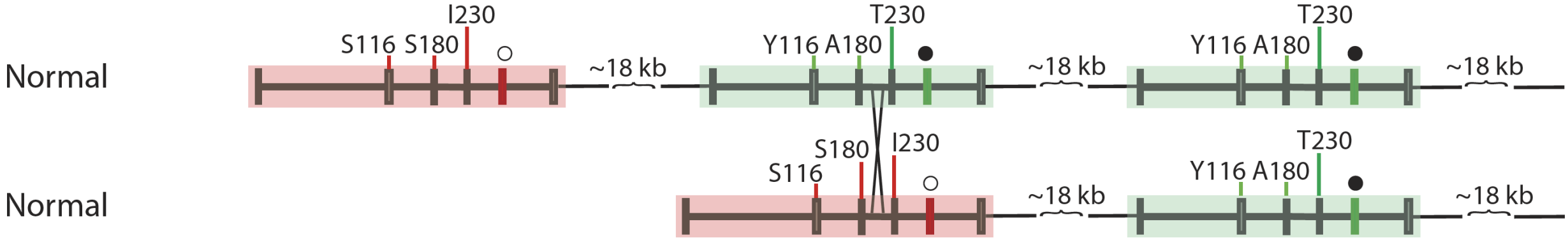
Anomalous trichromacies

- exist because there is variation in peak sensitivity of both L and M cone photopigments
- vary in severity according to spectral separation between underlying L or M pigments.


A
Absorption (percent of maximum)
100
80
60
40
20
0
450
500
550
600
650
Wavelength (nm)
L class
B
Absorption (percent of maximum)
100
80
60
40
20
0
450
500
550
600
650
Wavelength (nm)
M class
Xq28
OPN1LW
154,145,000
154,147,500
154,150,000
154,152,500
154,155,000
154,157,500
exon
amino acid
1
2
S 116
3
S 180
4
I 230
A 233
5
Y 277
T 285
Y 309
6
[~24 kb]
OPN1MW
154,185,096
154,187,596
154,190,096
154,192,596
154,195,096
1
2
Y 116
3
A 180
4
S 230
T 233
5
F 277
A 285
F 309
6


Normal
I230
S116 S180
~18 kb
T230
Y116 A180
~18 kb
Normal
I230
S116 S180
~18 kb
T230
Y116 A180
~18 kb

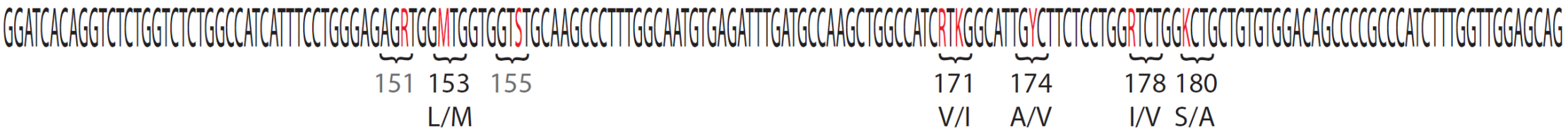

Normal
I230
S116 S180
~18 kb
T230
Y116 A180
~18 kb
Normal
I230
S116 S180
~18 kb
T230
Y116 A180
~18 kb


Normal
I230
S116 S180
~18 kb
T230
Y116 A180
~18 kb
T230
Y116 A180
~18 kb
Normal
S180
I230
S116
~18 kb
T230
Y116 A180
~18 kb

Recombination has intermixed the OPN1LW and OPN1MW gene sequences to an astonishing degree in humans

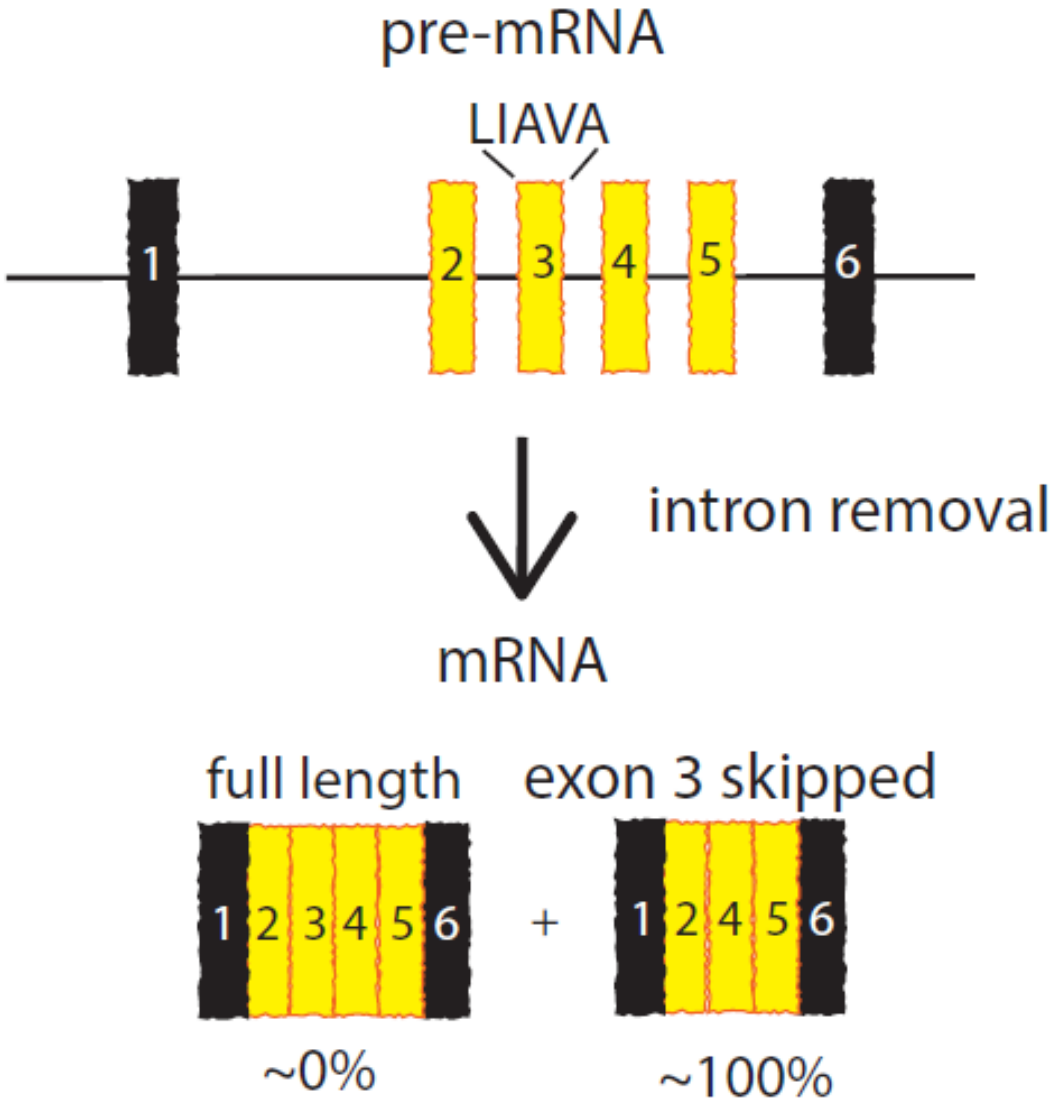
This coupled with altering the number of copies of opsin genes on the X-chromosome is a cause of

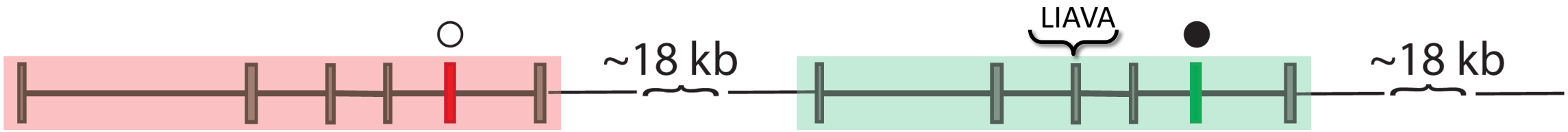
- blue cone monochromacy
- X-linked cone dytrophy
- Bornholm Eye Disease = a syndromic high grade myopia (nearsightedness) associated with red-green color blindness.


GGATCACAGGTCTCTGGTCTCTGGCCATCATTTCCTGGGAGAGRTGGMTGGTGGTSTGCAAGCCCTTTGGCAATGTGAGATTTGATGCCAAGCTGGCCATCRTKGGCATTGYCTTCTCCTGGRTCTGGKCTGCTGTGTGGACAGCCCCGCCCATCTTTGGTTGGAGCAG
151
153
155
171
174
178
180
L/M
V/I
A/V
I/V
S/A

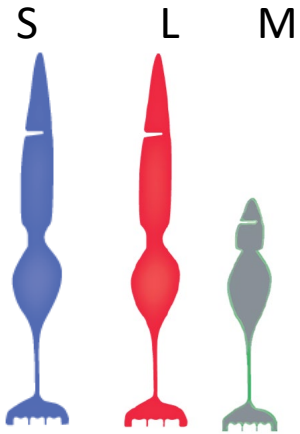
Exons carry instructions for splicing out the introns and joining the exons to create the protein code and information for making the opsin protein.

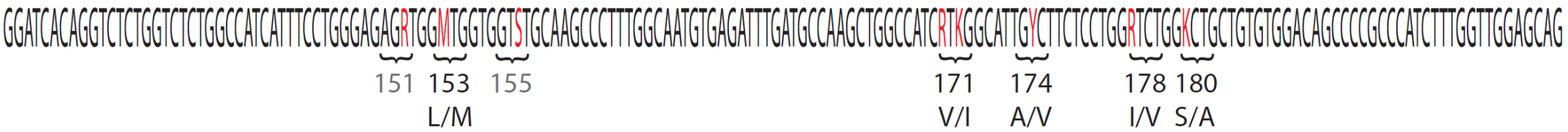
The LIAVA variant has lost the instructions for including exon 3 in the mRNA.



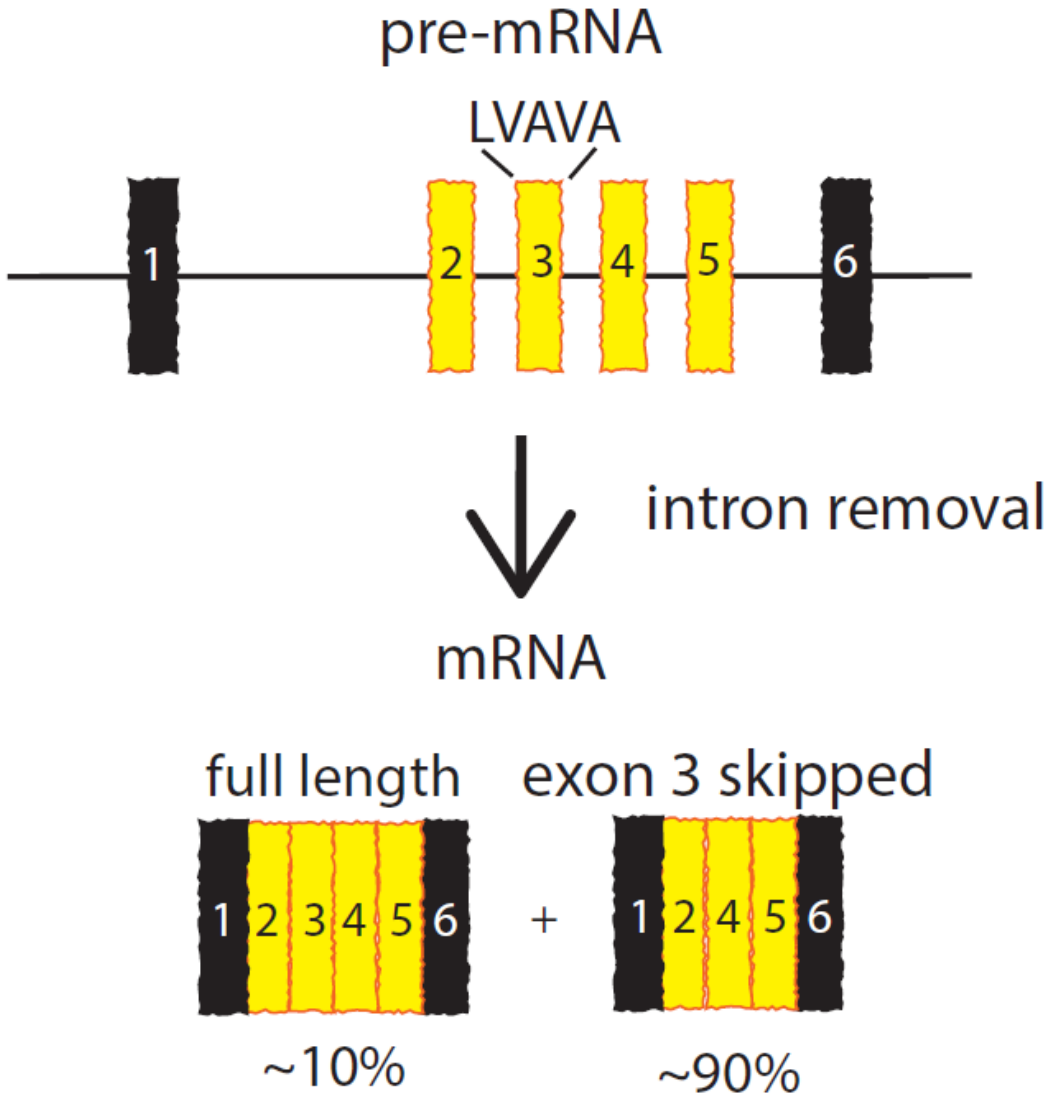


only L cones have pigment,
Phenotype = deuteranope

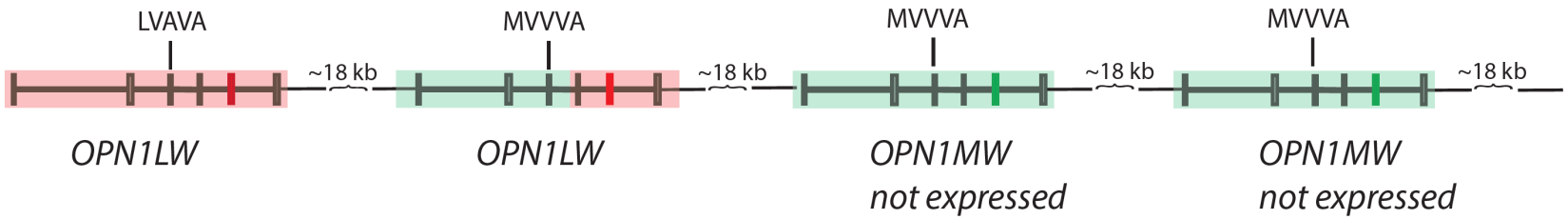


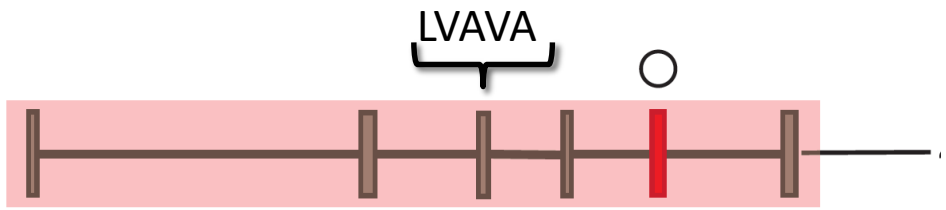

GGATCACAGGTCTCTGGTCTCTGGCCATCATTTCCTGGGAGAGRTGGMTGGTGGTSTGCAAGCCCTTTGGCAATGTGAGATTTGATGCCAAGCTGGCCATCRTKGGCATTGYCTTCTCCTGGRTCTGGKCTGCTGTGTGGACAGCCCCGCCCATCTTTGGTTGGAGCAG
151
153
155
171
174
178
180
L/M
V/I
A/V
I/V
S/A

LVAVA variants carries very weak instructions for including exon 3 in the mRNA.



A. Xq28 opsin gene array structure for affected males in original BED family





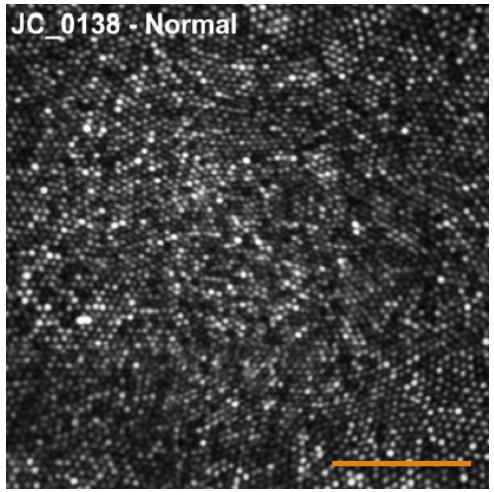
Phenotype

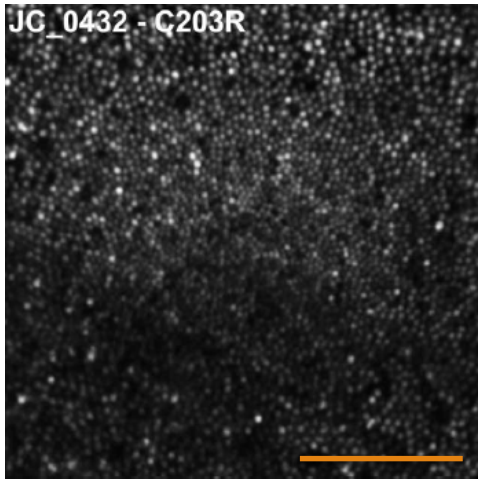
- Starts as dichromacy
- Eventually dichromacy with cone dystrophy
- Ultimately blue cone monochromacy

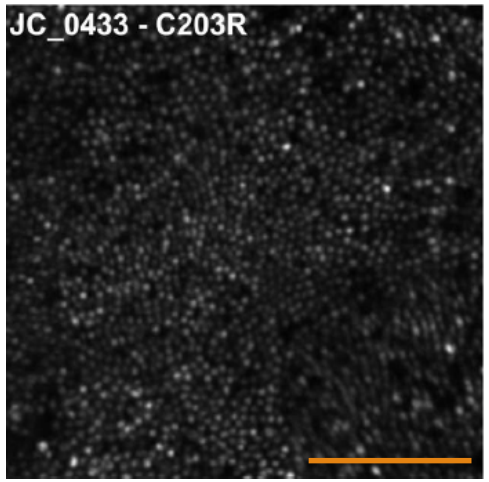
Rare, random amino acid changes have been identified as causes of dichromacy – and these can be associated with a loss of cone photoreceptors

Genotype: L_{C203R} M M
Phenotype: Protanope
This is associated with cone loss

Scale bars
= 100 µm







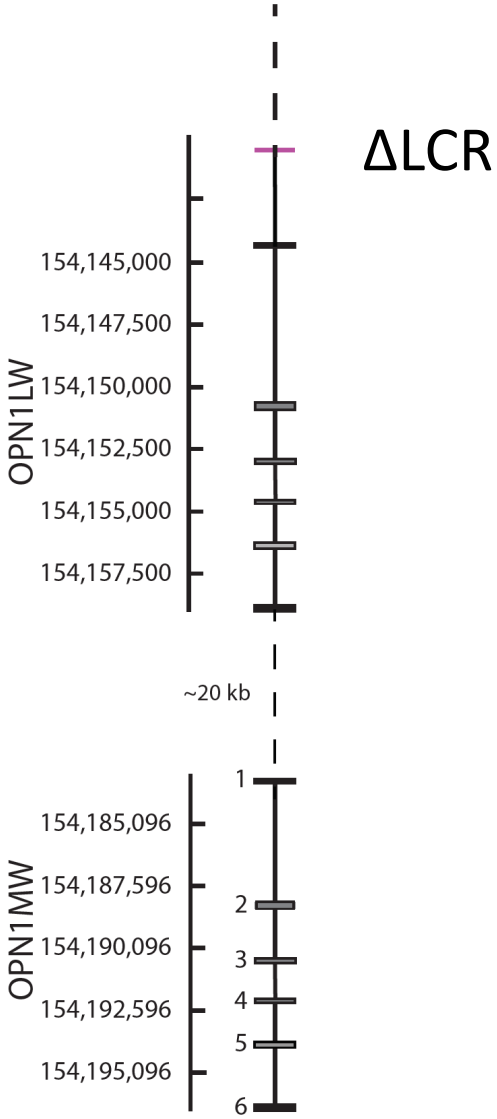
119,000 cones/mm^2

23,457 cones/mm^2

26,775 cones/mm^2

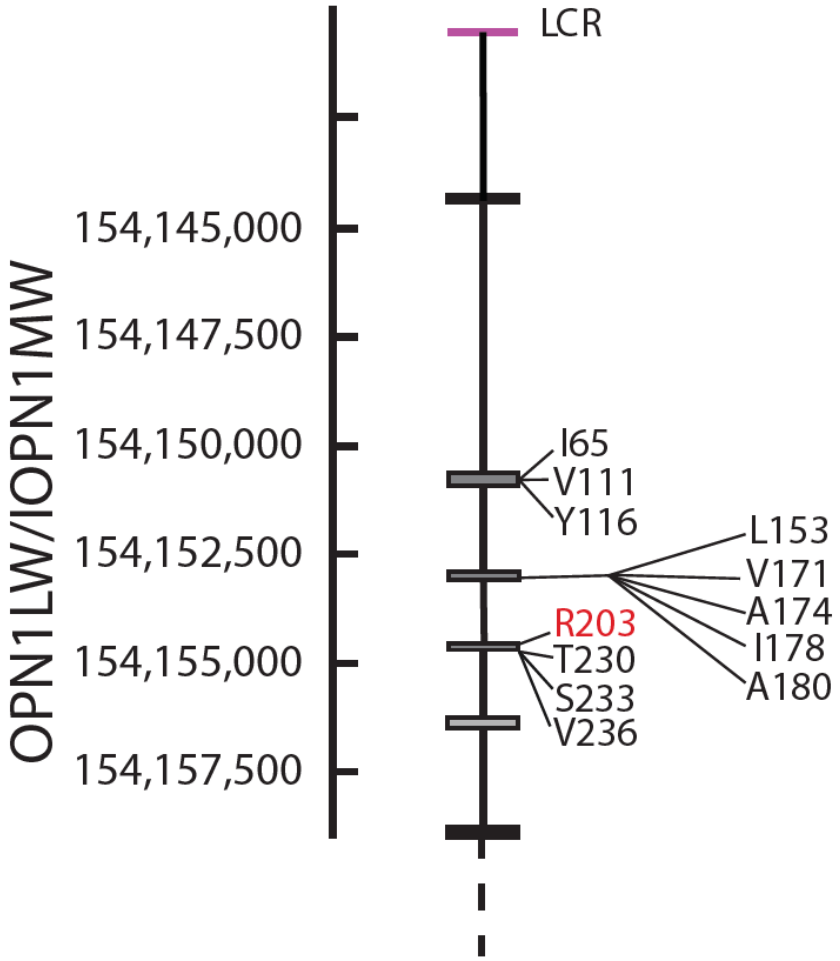
Blue Cone Monochromacy

- Vision is based on S cones and rods
- Only 6% of cones are S cones, so very poor acuity



LCR is enhancer ~3.7 kb upstream of array

Deletion of LCR prevents expression of all opsin genes on Xq28



- Deletion of all but one X-chromosome opsin gene
- Remaining gene has inactivating mutation
  - P307L
  - R247X
  - LIAVA

Cone opsin mutations

- Common red-green color vision deficiencies
- Tritan color vision deficiency
- Blue cone monochromacy
- X-linked cone dystrophy/X-linked cone dysfunction
- High grade myopia

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