Retinitis Pigmentosa

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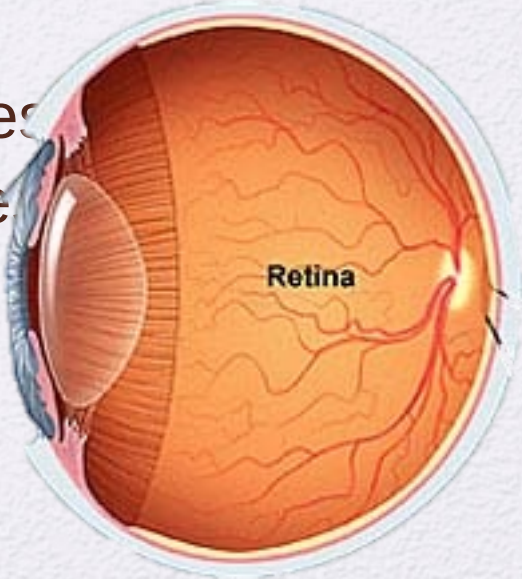
Retinitis Pigmentosa

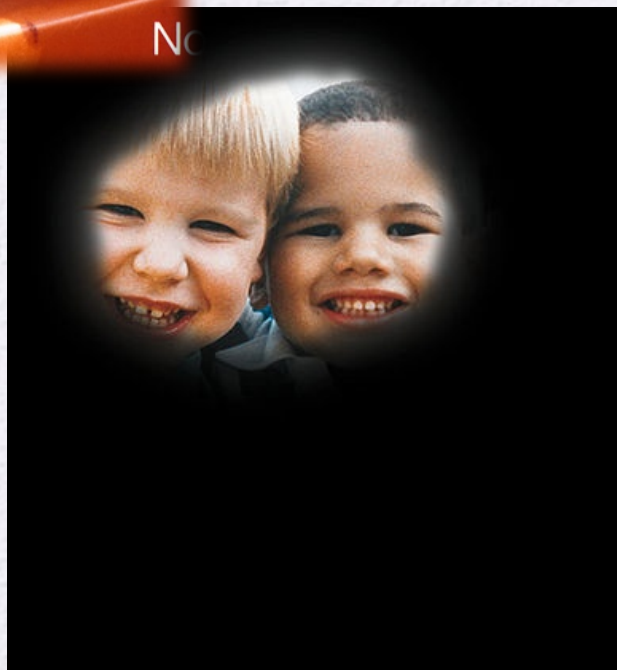
- One of the most common inherited retinopathies
- ~ 1/3500 (0.03%) of people in US and Europe have some form of RP
- Genetically heterogeneous:
  - Autosomal recessive (50-60% of cases)
  - Autosomal dominant (30-40% of cases)
    - **<u>RP4</u> accounts for 15% of adRP**
      - **P23H on chromosome 3**
  - X-linked (5-15% of cases)



Symptoms of RP4

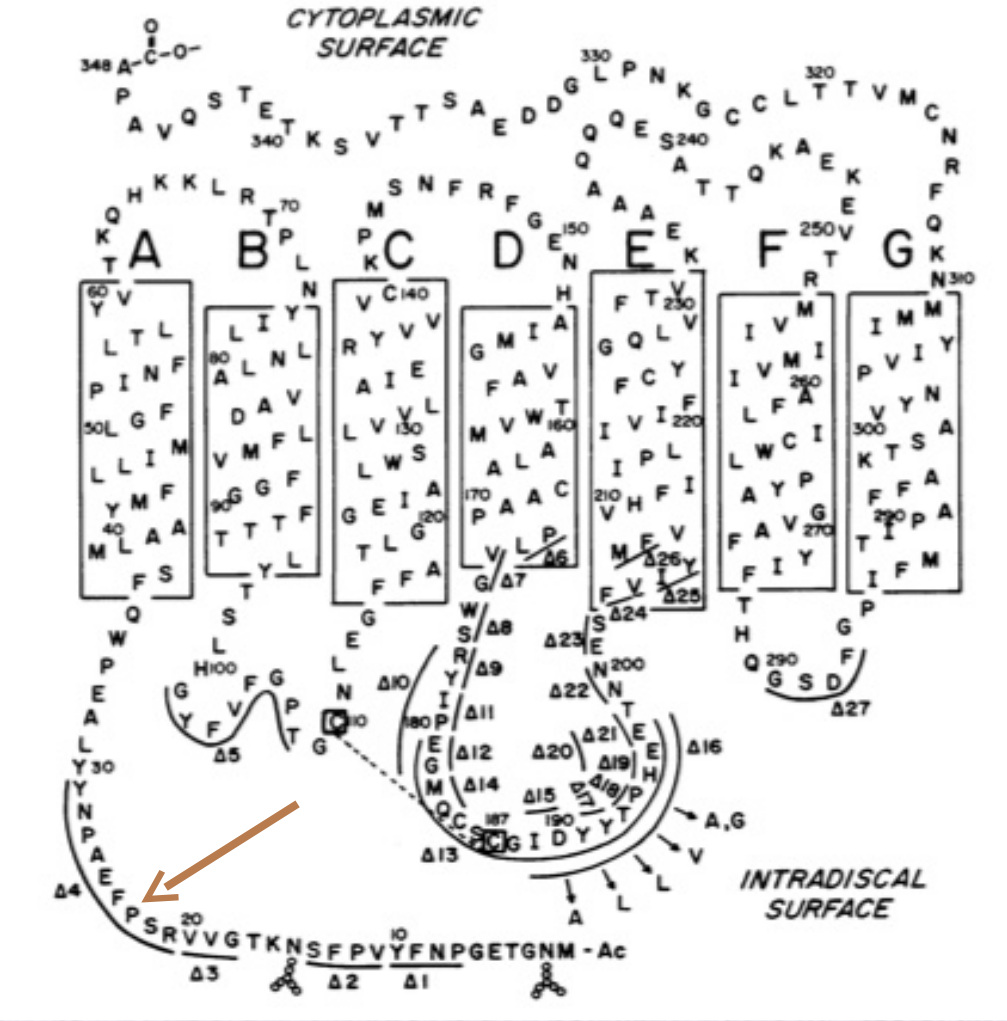
- A rod-cone dystrophy (degeneration), progressing in 3 stages:
  - Nyctalopia / defective dark adaptation / “night blindness” (early stage)
  - Loss in the peripheral visual field in daylight / “tunnel vision” (mid stage, progressive)
  - Complete blindness (end stage, in worst cases)

Normal vision

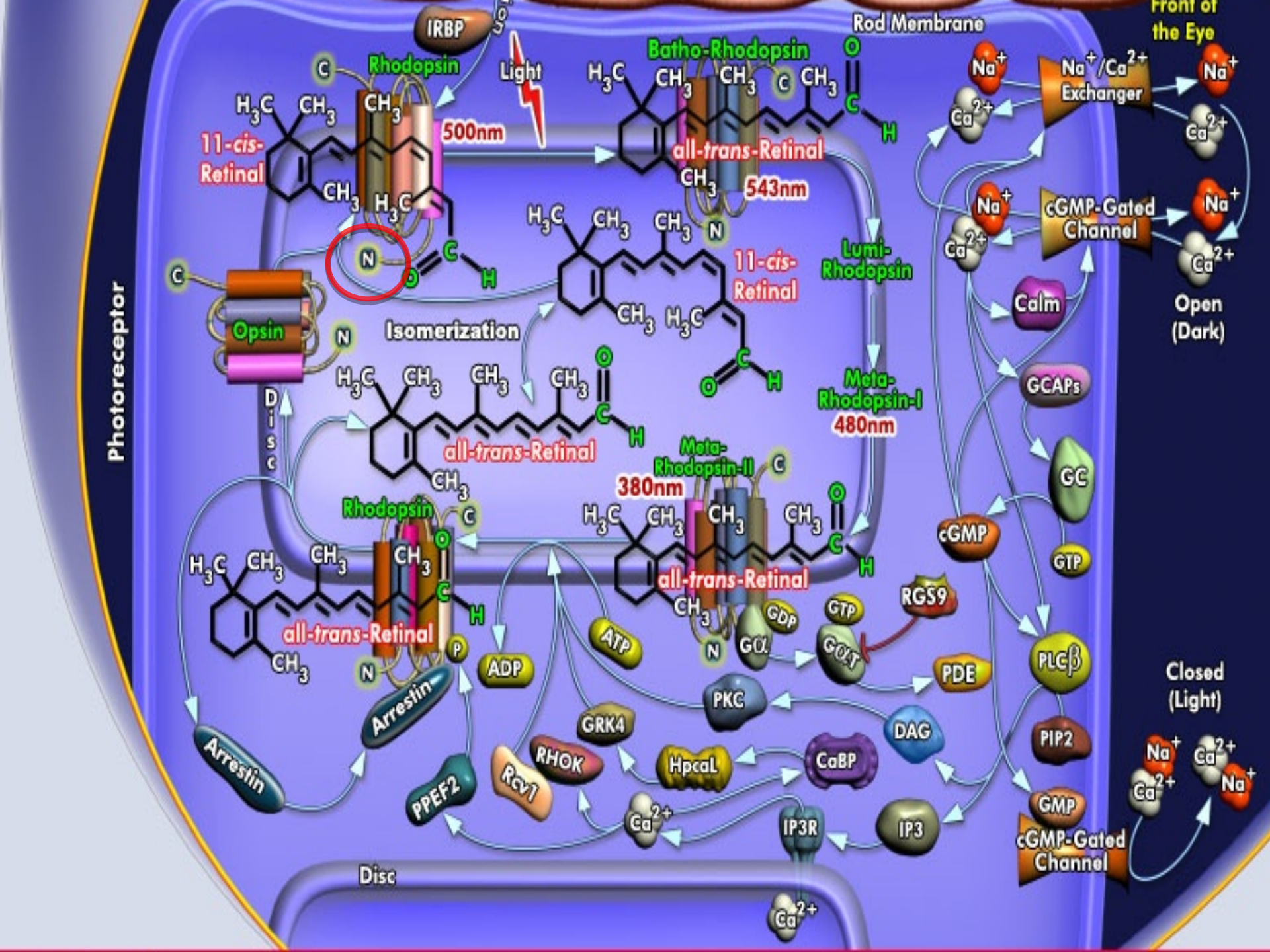


RP “tunnel vision”

Biochemistry of RP4

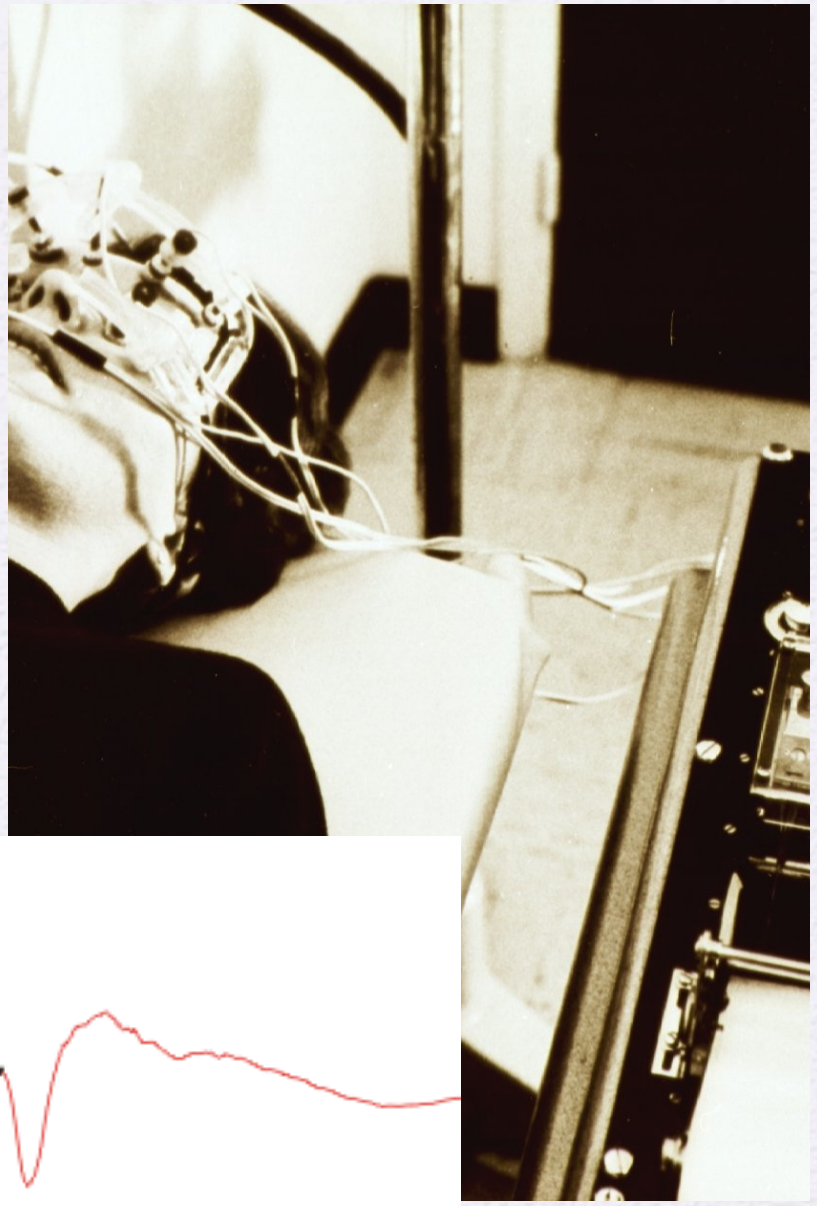


- This is a single amino acid change of Proline (nonpolar, neutrally-charged) to Histidine (polar, positively-charged 10% of time) on the N-terminus of the intradiscal surface of the rhodopsin protein


Photoreceptor
Disc
IRBP
Rhodopsin
11-cis-Retinal
500nm
Light
Batho-Rhodopsin
all-trans-Retinal
543nm
Rod Membrane
Front of the Eye
Na+/Ca2+ Exchanger
Na+
Ca2+
cGMP-Gated Channel
Open (Dark)
Opsin
Isomerization
Lumi-Rhodopsin
Calm
GCAPs
Meta-Rhodopsin-I
480nm
Meta-Rhodopsin-II
380nm
GC
cGMP
GTP
RGS9
GDP
GTP
Gα
Gαt
PDE
PLCβ
ATP
ADP
PKC
DAG
PIP2
GRK4
RHOK
HpcaL
CaBP
Rcv1
PPEF2
Arrestin
IP3R
IP3
GMP
Closed (Light)

Classical Diagnosis of RP4

- Electroretinography
- Posterior subcapsular cataracts
- Dust-like particles in the vitreous
- White dots deep in the retina
- Intraretinal clumps of black pigment
- Attenuated retinal vessels
- Loss of RPE
- Visual field testing



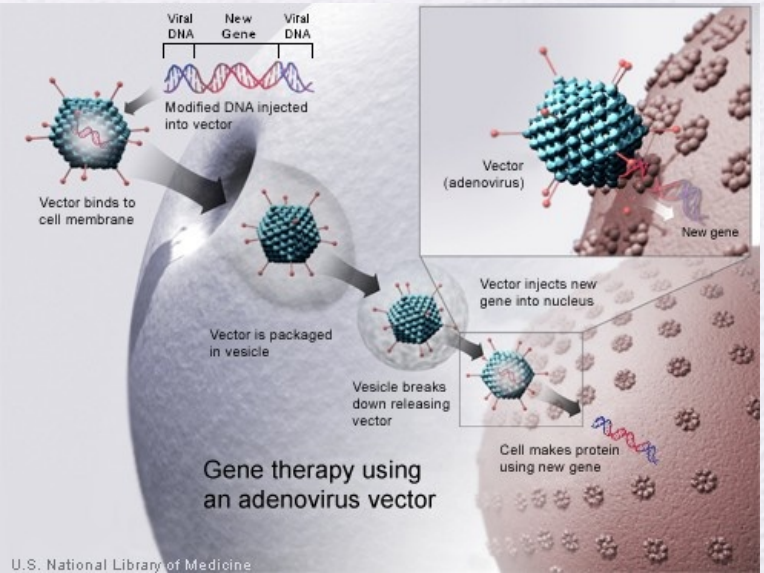
Classical Treatment of RP4

(There is no definite cure for RP4)

- Cataract extraction
- Vitamin A supplements / instruction to eat more foods containing vitamin A
- Fetal neural retinal transplantation (unsuccessful)
- Photoreceptor transplantation from cadaver (unsuccessful)
- Retinal prosthesis (*slight* improvement)

Novel Diagnostics & Therapies for RP4

- Diagnostics:
  - Molecular genetic testing
    - Available for 11 possible mutations
  - Genetic counseling
- Therapies:
  - Intravitreal or [illegible] therapy
    - Use of adenovirus or lentivirus vector to replace defect in identified forms of RP
    - [illegible]mpossible in RP4



References

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