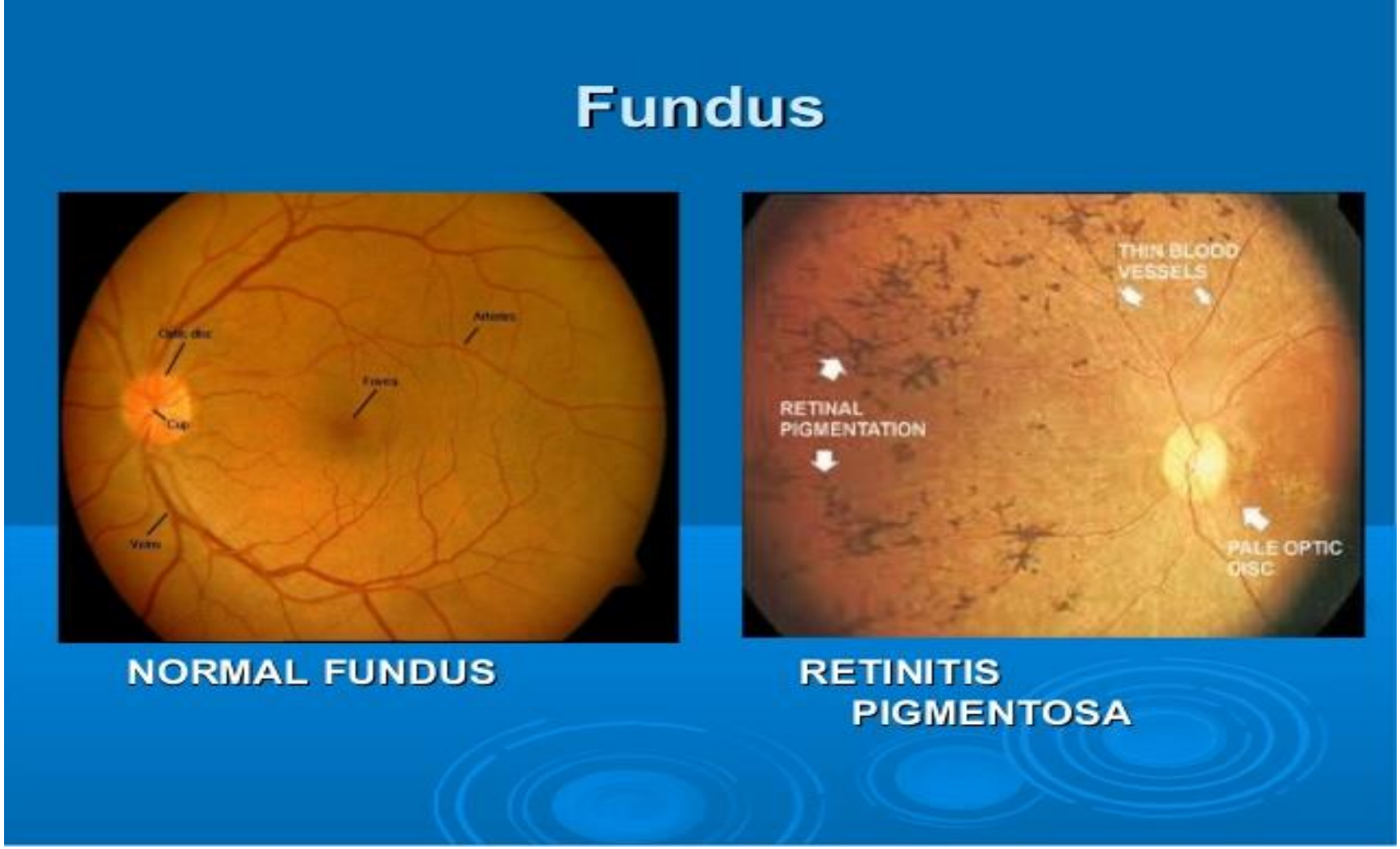
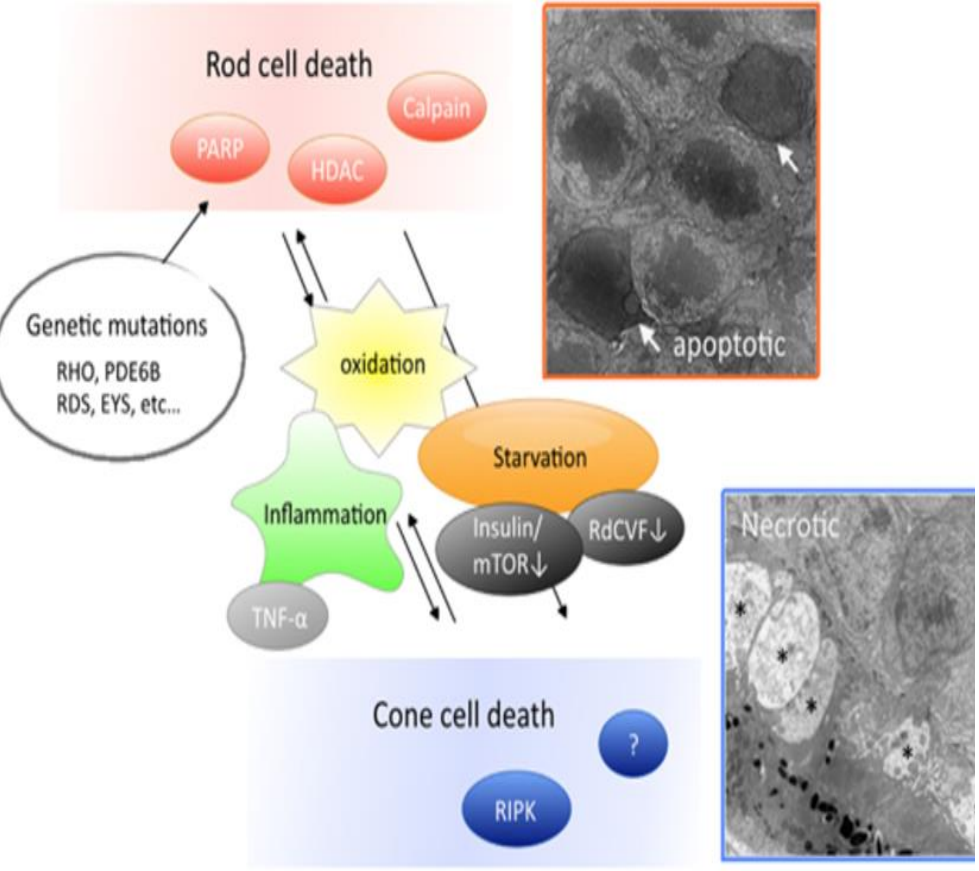
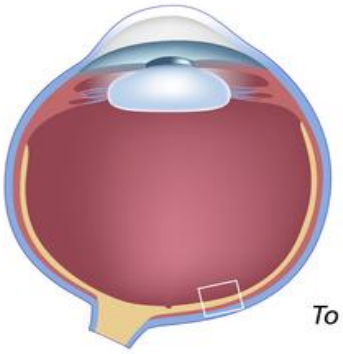
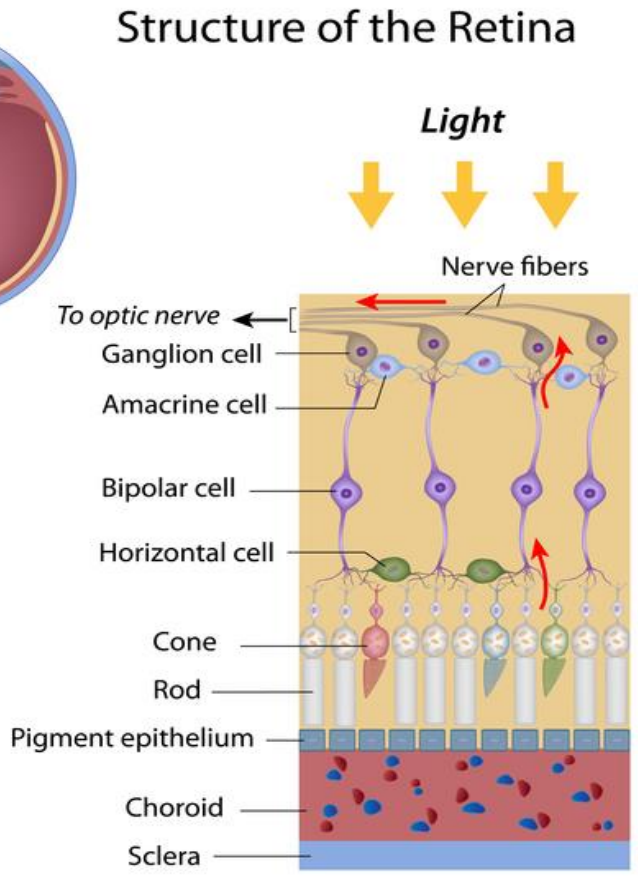


RETINITIS PIGMENTOSA A RARE GENETICAL DISORDER

Retinitis pigmentosa (RP) is a group of inherited disorders affecting 1 in 3000-7000 people and characterized by abnormalities of the photoreceptors (rods and cones) or the retinal pigment epithelium of the retina which lead to progressive visual loss. RP can be inherited in an autosomal dominant, autosomal recessive or X-linked manner. While usually limited to the eye, RP may also occur as part of a syndrome as in the Usher syndrome and Bardet-Biedl syndrome. Over 40 genes have been associated with RP so far, with the majority of them expressed in either the photoreceptors or the retinal pigment epithelium.The disease leads to progressive degenaration of the retina.



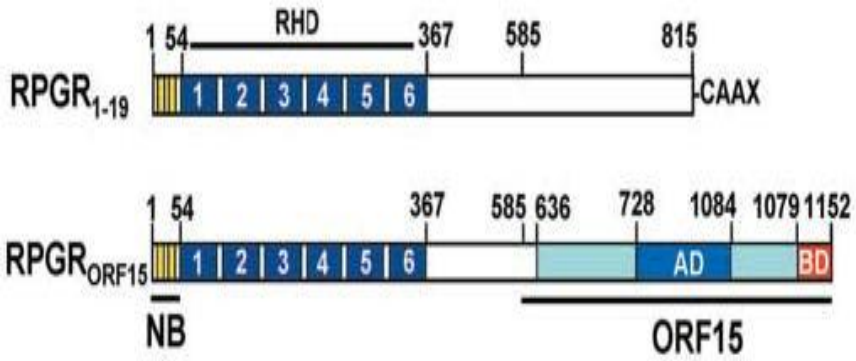




Rod and cone cell death in retinitis

Apoptosis and necrosis are two forms of cell death . Necrosis was traditionally considered as an unregulated form of cell death, it is now known to have regulated components, such as those involving receptor-interacting protein (RIP) kinases.Rod and cone photoreceptor cell death in retinitis pigmentosa. Rod cell death due to the deleterious genetic mutations is associated with apoptosis, which involves the activation of caspase-independent pathways including poly-ADP-ribose-polymerase (PARP), calpain and histone deacetylase (HDAC). Cone cell death is induced by the microenviromental changes subsequent to rod degeneration, such as oxidation, inflammation and loss of trophic factors. Dying cones show different morphological features from rod cells, such as necrotic cytoplasmic swelling (asterisk), and is partly mediated through the activation of RIP kinase (RIPK). Electron microscopy images were reproduced with permissions from Murakami et al.5 mToR, mammalian target of rapamycin; RdCVF, rod-derived cone viability factor; TNF-α, tumor necrosis factor-α.

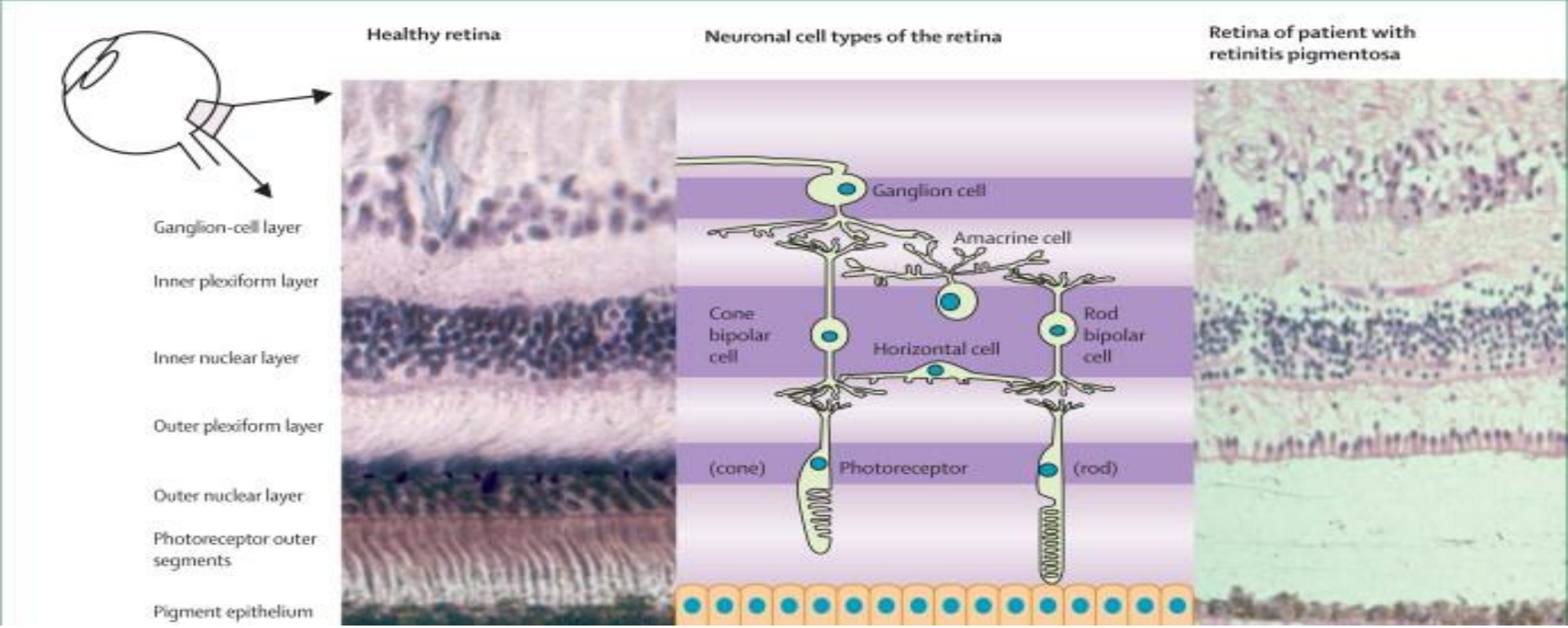
X-linked retinitis pigmentosaX-linked RP (XLRP) is one of the most severe forms of human retinal degeneration, as determined by age-of-set and progression, and accounts for six to 20 % of all RP cases. At least six XLRP loci have been identified, but RP3 is the major subtype of XLRP, accounting for 70 to 80 % of affected families. The RPGR gene is responsible for the RP3 form of XLRP and is mutated in 10-20 % of all RP patients. The pathogenesis of retinitis pigmentosa GTPase regulator (RPGR) mutant-causing RP is not clear, different animal models have been used to understand the pathogenesis of these diseasesPatients with this form of retinitis pigmentosa present with symptoms of night blindness from childhood; they have progressive constriction of visual fields and loss of vision in mid-life, although the severity of the disease does vary. The gene for this condition has been mapped to Xp11.3 (short arm of the X chromosome). Further evidence also maps the X-linked gene to Xp21, particularly in families where the female carrier demonstrates the golden tapetoretinal reflex. Recently these gene loci have been designated *RP2* (Xp11.3) and *RP3* (Xp21.1). Currently, probes are available for identifying both loci and may be used for prenatal diagnosis and genetic counselling. RPGR interacts with the RPGR interacting protein-1 (RPGRIP1). Mutations in *RPGRIP1* cause Leber's congenital amaurosis.



Primary structure of RPGR isoforms. $RPGR_{1-19}$ is encoded by the constitutive exons 1–19 of *RPGR*. $RPGR_{1-19}$ contains a functional, C-terminal isoprenylation site. $RPGR_{ORF15}$ is encoded by the constitutive exons 1–15 and intron 15. The constitutive exon 15 and intron 15 encode ORF15. The ORF15 contains a repetitive and very acidic domain (AD) and a small C-terminal basic domain (BD).The picture is shown beside.

Autosomal dominant retinitis pigmentosa:

several mutations have been found in candidate genes in up to 30% of patients with autosomal dominant retinitis pigmentosa. Mutations in two genes have been studied in particular. These are the rhodopsin gene on chromosome 3q (accounting for 20% of all cases) and the peripherin gene on chromosome 6p. The rhodopsin molecule, composed of 348 amino acids, exists as a seven-loop transmembrane protein in the rod outer segment. The C-terminus of the protein is in the cytoplasm and the N-terminus of rhodopsin is in the intradiscal space. Throughout the protein, several regions are affected by mutations, which fall into three main groups: mutations affecting amino acids in the intradiscal space; mutations affecting amino acids in the transmembrane domain; and mutations affecting amino acids in the cytoplasm. Most of these mutations probably destroy the three-dimensional (tertiary) conformation of the protein and in some way affect protein function. To date, over 150 different mutations have been reported, the majority of which are point mutations, although deletions have also been discovered.A recent study found that mutations in the NRL gene associated with dominant retinitis pigmentosa. Mice lacking the transcription factor Nrl have no rod photoreceptors and an increased number of short-wavelength-sensitive cones. Missense mutations in NRL are associated with autosomal dominant retinitis pigmentosa; however, the phenotype associated with the loss of NRL function in humans has not been reported. **T**he *NRL* gene encodes a basic motif-leucine zipper protein, which is a member of the Maf transcription factor family . In the adult retina, NRL is expressed in rod photoreceptors where it functions synergistically with the cone-rod homeobox transcription factor CRX to stimulate the expression of several proteins of the phototransduction cascade such as rhodopsin and the α and β subunits of rod-specific phosphodiesterase**.AUTOSOMAL RECCESIVE RETINITIS:** This form of RP tends to show first signs between 30 and 40 years and tends to cause more severe sight loss.

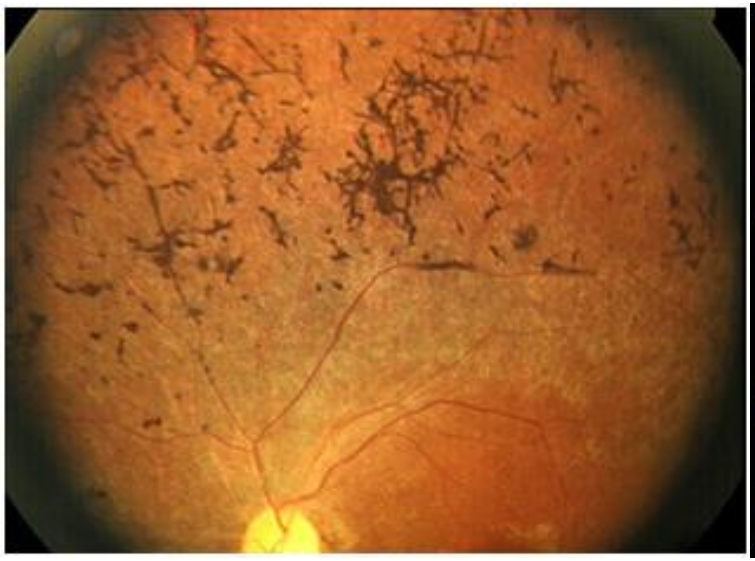


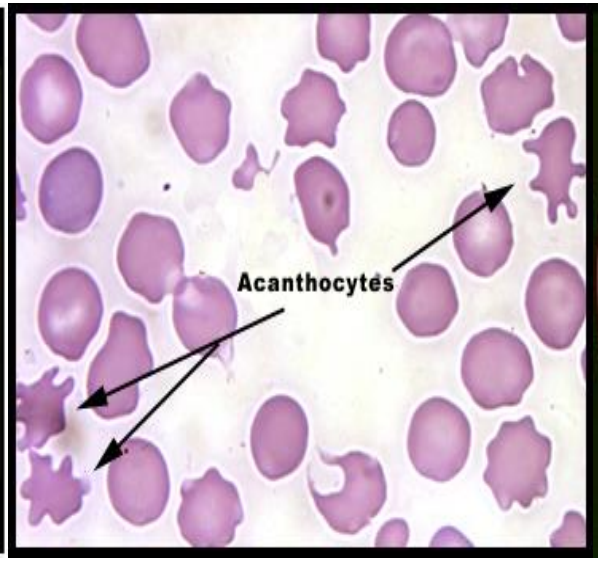
SYMPTOMS

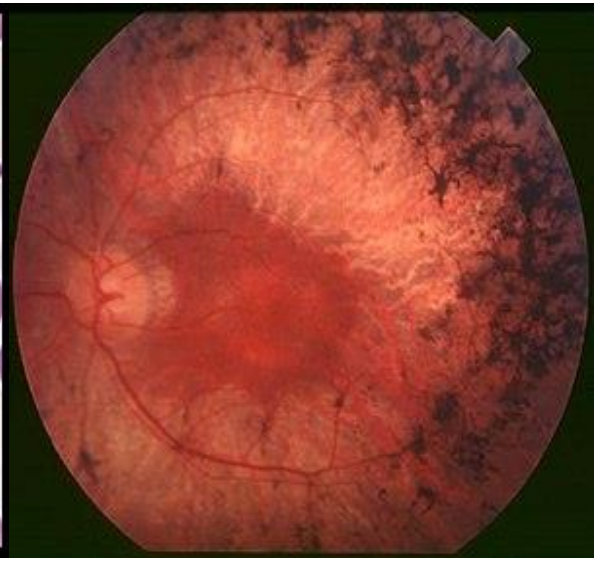
In most of the more common forms of RP, the first symptoms occur between childhood and the age of 30. The first symptom you usually notice is that you find it difficult to see in poor light, such as outdoors at dusk, or in a dimly lit room. This is often referred to as “night blindness”. While most people find it takes their eyes about 20 minutes to adapt to dim light, if you have RP it will either take much longer or it won’t happen at all. A second symptom is the loss of some of your peripheral vision or peripheral visual field. This means that when you’re looking straight ahead you become less able to see things either to the side, above or below. Difficulty seeing in low light and loss of peripheral vision are a sign that the peripheral rod cells are being affected by RPIn some RP-related conditions, central vision is lost first because the central cone cells are affected first. You might find it difficult reading print or carrying out detailed work at this time. In these types of RP, peripheral vision is affected in the later stages. Later symptoms All RP conditions are progressive, but the speed and pattern of deterioration of sight varies from one person to another. For most people, the first effect of RP is the gradual loss of peripheral vision. This means that you can start to miss things slightly to the side of you or trip over or bump into things you would have seen in the past. Most people with RP eventually have a very restricted visual field, leaving only a **narrow tunnel of vision**. Most people with RP retain useful central vision through their twenties, which means the ability to read and recognise faces is not greatly affected. By 50 years of age most people’s central vision is affected to the extent that reading is a problem without the help of a magnifier. Many people who have RP find the glare from bright lights and sunlight becomes an increasing problem. The retinal cells become less able to adapt to changing light levels and it becomes more difficult to use your vision when you move between a light and a dark room.

RETINITIS PIGMENTOSA ASSOCIATION WITH OTHER DISEASES

Retinitis pigmentosa is also found in association with anosmia, ataxia, dry skin, and EKG abnormalities with elevated serum phytanic acid (Refsum disease); malabsorption, acanthocytosis, ataxia, and abetalipoproteinemia (Bassen–Kornzweig syndrome); and adult-onset ataxia, dysarthria, hyporeflexia, decreased proprioception, decreased vibration sense, and low serum vitamin E levels (Friedreich-like ataxia with retinitis pigmentosa). These uncommon recessively inherited conditions are treatable as follows: a low phytol/low phytanic acid diet (excluding animal fats, milk products, and dark green leafy vegetables) in the case of Refsum disease; a low-fat diet plus supplementation with vitamin A, vitamin E, and vitamin K in the case of Bassen–Kornzweig syndrome, and vitamin E supplementation in the case of Friedreich-like ataxia associated with retinitis pigmentosa.

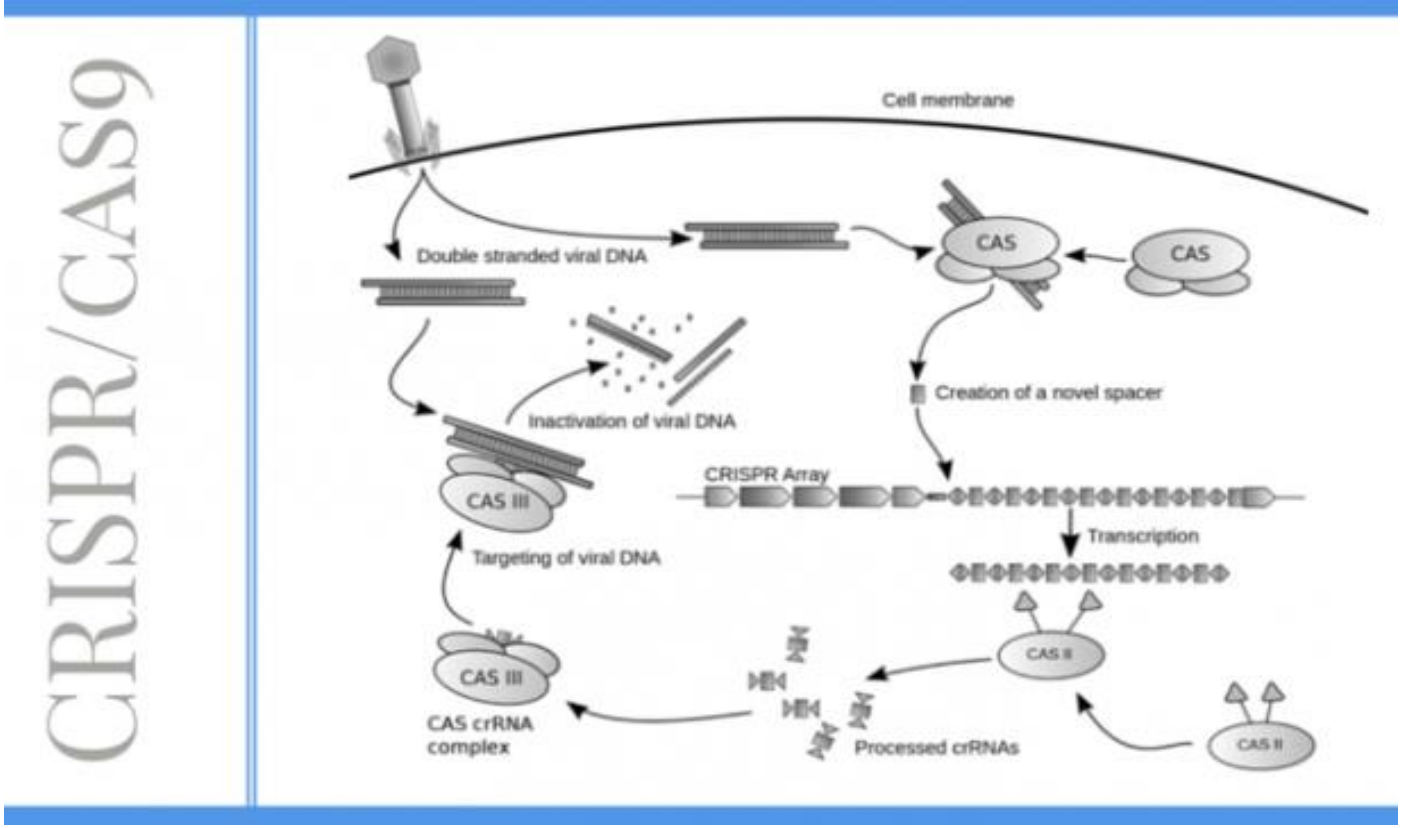






VITAMIN A-SUPPLEMENTS: Vitamin A plays a crucial role in the biochemistry of visual signal cascade and the maintenance of an optimal vitamin A status has been considered relevant for a normal retinal physiology. In an animal model of RETINITIS PIGMENTOSA patients seems to get beneficial effects from a supplementation with vitamin A, since it has been associated with an improved preservation of cone electroretinogram amplitudes and has been proposed as a treatment to slow the progression of the disease . Moreover, for RP patients assuming vitamin A therapy addition of the polyunsaturated fatty acid docosahexaenoic acid has been showed to slow the course of the disease over the first two years of supplementation . Similarly, an increased dietary intake of lutein, a retinal carotenoid, seems to slow visual function loss in RP adult patients assuming vitamin A . Most adults with blinding retinitis pigmentosa (RP) should take adaily, 15,000 IU vitamin A supplement.Studies have shown that an average patient who started taking a 15,000 IU vitaminA capsule at age 32 would retain some useful vision until age 70,whereas a patient not on this dose would lose useful vision at age 63.Study also shows that the disease appeared to progress faster on average in patients on a daily, 400 IU vitamin E supplement than in those taking a trace amount of the vitamin.though there is no evidence that normal dietary or small supplemental amounts of vitamin E have an adverseeffect on the disease.A study of 357 patients shows that taking 15,000 IU/day of vitamin A as retinyl palmitate for 4–6 years, those with a diet high in long chain omega-3 fatty acids (≥0.20 g/day) had a 40% slower mean annual rate of decline in distance visual acuity than those with a diet low in these fatty acids.

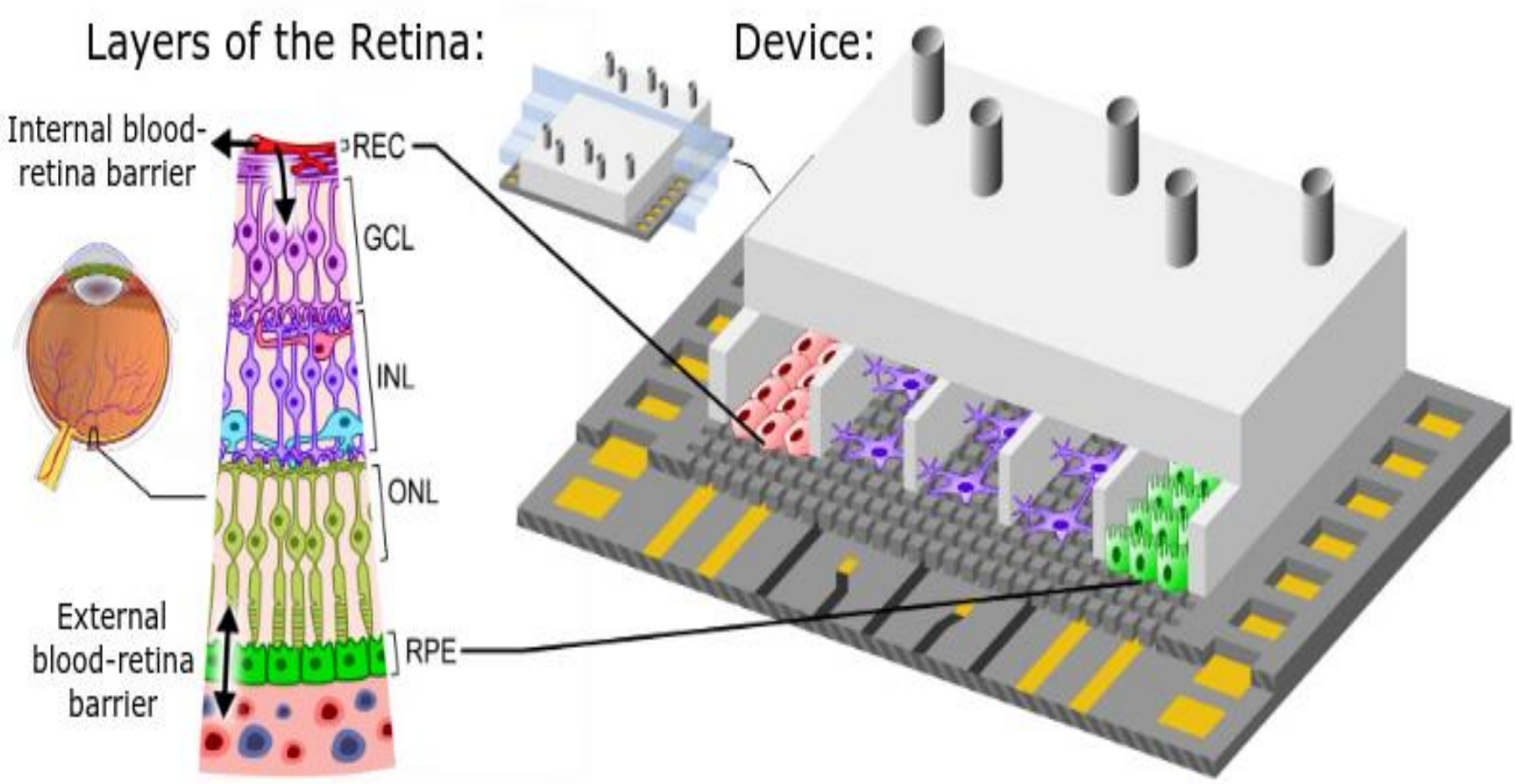
Iodine may alleviate swelling in retinitis pigmentosa patients' retinas: Cystoid macular edema (CME) is a common complication of retinitis pigmentosa. Researchers of Medicine tested whether the extent of retinal swelling due to CME was inversely related to dietary iodine intake in patients with RP and found that it was. This finding raises the possibility that an iodine supplement could help limit or reduce central foveal swelling in RP patients with CME



A NEW GENE EDITING METHOD FOR CURING RETINITIS PIGMENTOSA

A revolutionary new technology called CRISPR, designed for gene-editing, is being used to research a possible treatment for retinitis pigmentosa (RP) by Columbia University Medical Center and the University of Iowa. Researchers successfully used the CRISPR technology to repair the defective genes of a rat. This is exciting because the potential lies in the possibility that these repaired genes can now be placed back into the donor eye as a cure for retinitis pigmentosa. It could very well be the first personalized treatment for humans in the future with a lessened fear of the body rejecting the edited cells since they are going back into the original donor. Other eye diseases caused by mutated genes could also be treated using the same method as well.

The CRISPR technology is not yet approved for human use but steps are being taken so that it can possibly be approved one day in the near future.

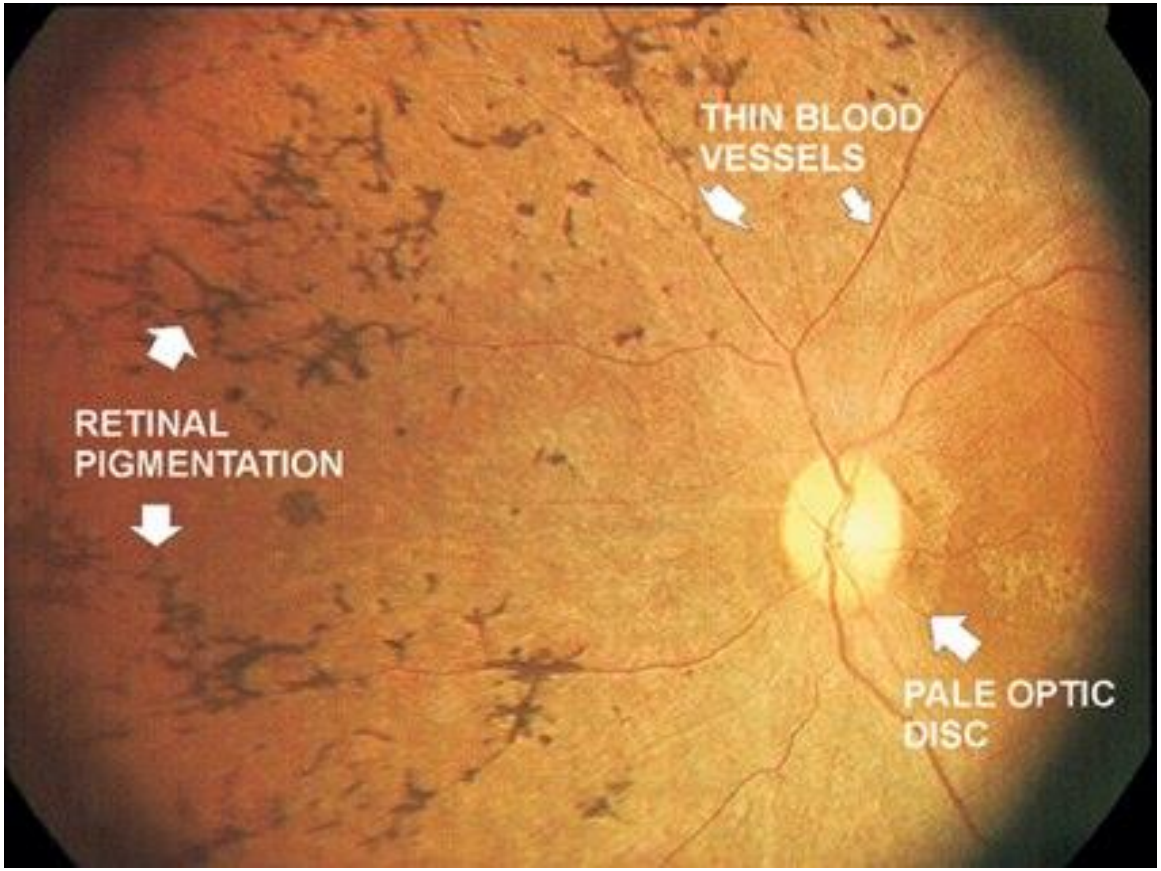


A new device for the treatment of retinitis

A new 'organ-on-a-chip' device for the blood-retina barrier could speed up the development of treatments for eye diseases like retinitis pigmentosa.

Researchers from Microelectronics Institute of Barcelona, Vall d'Hebron Research Institute, and Universitat Autònoma de Barcelona have developed a **microfluidic chip** that mimics the human **blood-retinal barrier** in the eye. The study, published in *Lab on a Chip*, sets out how the design of the device replicates the structure of the retina.

The device is composed of **several parallel compartments** that recreate the layered structure of the retina. In each compartment, a **specific cell type** is grown to replicate the different layers as closely as possible. For example, **endothelial cells** represent capillaries, neurons take the place of the neuroretina, and **retinal pigmented epithelial cells** make up the device's external blood-retinal barrier.



conclusion

Retinitis pigmentosa is a very rare genetical disorder and new researches are trying to cure the disease.Though some of the technologies are invented to cure the disease but still more studies and development needed to be done on this particular disease.