REVIEW ARTICLE



The role of melanin in retina detachment

Arturo Solís Herrera, María del Carmen Arias Esparza, Paola Eugenia Solís Arias

Human Photosynthesis(TM) Research Centre, López Velarde 108, Centro, Aguascalientes 20000, México

ABSTRACT

Retinal adhesiveness mechanisms in mammals are quite complex and multifactorial in nature. To date, the role played by the various anatomical structures that surrounding the retinal tissue, such as retinal pigment epithelium, interphotoreceptor matrix, the vitreous body, and sclera is poorly understood due to the diversity of biophysical forces and biochemical interactions that impinging upon retinal tissue in regards form and function. The adhesion of the retina to the choroid, rather than anatomical, is a dynamic process, as the retina detaches a few minutes after the life ceases. The adhesion mechanisms are described more frequently in the literature such as intraocular pressure and the oncotic pressure of the choroid that seem to push the retina toward the choroid, the delicate anatomical relationships between the photoreceptors (rods and cones) and the RPE; the existence of a complex material called interphotoreceptor matrix as well as other metabolic and structural factors cannot explain by themselves or together the remarkable features observed in the adhesion process between the photoreceptor layer and RPE cells. The unexpected intrinsic property of melanin to absorb light energy and transform into chemical energy explains very well normal adhesion of the sensory retina to the pigment epithelium. In this article, we offer, in a comprehensive way, the explanation.

Key words: Choroid layer, melanin, retina detachment, vitreous body, water dissociation

INTRODUCTION

ammalian eye consists, in its posterior part, of three concentric layers of tissues that contain melanin pigment in different proportions and whose anatomical pattern is repeated in all or almost all species. Broadly speaking, the eye consists, in its anterior part, of transparent structures (cornea, lens, and vitreous) that allow passage of light between 300 and 600 nm, which operate in the manner of positive lenses that focus the light beams so that a recognizable image is formed on a photosensitive tissue or more exactly photoreceptor which is provided immediately before a tissue with a significant amount of melanin.

The brain linear dimension scales with the 0.22 power of the animal weight (Schmidt-Nielsen, 1984). Since the retina is a part of the brain, its diameter should also scale with the 0.22 of body weight, and the other dimensions of the eye, such as axial length, may scale with weight in the same way [Figure 1].

In the different species, there is a curvilinear relationship between the logarithm of axial length and the logarithm of body weight,^[1] which can be stated in the following form:

Axial length (mm)=10.61*Weight (kg)^{0.1964}

The radius of curvature, refractive power, and diameter of the transparent tissues (i.e., cornea and crystalline lens) are variable, but finally a clear image on retina is a major determinant. The morphological characteristics of the photoreceptors (rods and cones) are environment depending, but what is unchanging is the ever presence of melanin [Figures 2 and 3].

A longer eye has a greater resolving power, besides that the increased distance between the cornea/lens and the retina increases the size of the image. A large image is quite useful for animals that rely on vision to find food and escape from predators. For a more detailed review of eye size characteristics in different animal species see Howland *et al.*, 2004.

Address for correspondence:

Human Photosynthesis(TM) Research Centre. Lopez Velarde 108, Centro, Aguascalientes, Aguascalientes, México. CP 20000. E-mail: comagua2000@yahoo.com

© 2018 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

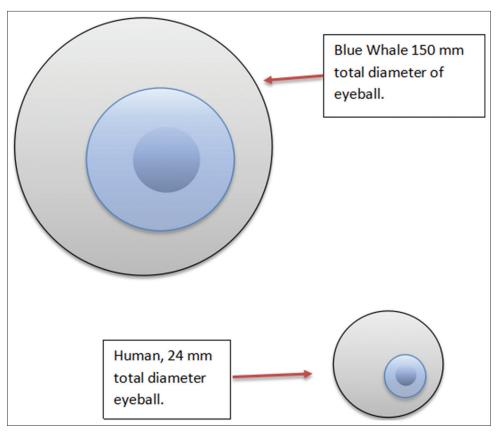


Figure 1: It is known empirically that the brain weight scales with 0.66 power of the body size in many vertebrates

ANATOMY OF VITREOUS BODY

The vitreous body, in the surface, has a condensation termed the inner limiting membrane and also the basal lamina of the retina. It is a thin, acellular and lines the inner retinal surface. With the light microscope, it appears as a single layer that is thick posteriorly and thin near the ora serrata. With the electron microscope, the inner limiting membrane is seen as a felt-like structure of delicate collagen-like fibrils in a dense matrix. The membrane is 1000–2000 Å thick and shows an irregular outer surface. It has a flat inner surface in which delicate collagen-like fibrils of the vitreous cortex are inserted.^[2] Numerous coarse vitreous fibers oriented perpendicularly and attached to the membrane surface are present in the vitreous base [Figures 4 and 5].

Vitreous structure eluded investigators, because the difficulty in confirming, with ordinary histologic techniques, observations made with biomicroscope in the live patient. However, the vitreous body has a fibrous framework consisting of fibers that form sheet-like aggregates. Histochemical studies show that these fibers are collagenous, $3-5 \mu$ thick, and contain fine fibrils.^[3]

The vitreous base, in phase-contrast microscopic studies, appears as a complex system of fibers originating in the region of the posterior pars plana ciliaris and the ora serrata. These fibers are attached to the inner limiting membrane and are often oriented perpendicularly to it. They appear as closely interlacing fibers which form bundles fanning out into the vitreous gel. The vitreous base has a firm adhesion to the peripheral retina through collagen-like fibrils that penetrate the limiting membrane and become attached to the Müller cells through plaque-like condensations in the cytoplasm.^[4]

Collagen-like fibers are the most important component of the vitreous. Vitreous cells, termed hyalocytes, occur normally in the vitreous cortex. Mucopolysaccharides are a third component of the vitreous body and cortex and occupy the spaces between the fibers.

Vitreous body is a "liquid tissue" that shows different types of alterations. The most frequent is liquefaction, where the collagen network losts its complex organization and optically empty spaces developed through the vitreous all. Calcium compounds appearing distributed along the vitreous body are also a common finding; however, its relationship with systemic diseases is poorly understood [Figures 6-8].

With age, shrinking of vitreous body seems a natural trend but results in tension on the retina. It is very frequently examination finding during ophthalmoscopy and usually is not dangerous. However, if the vitreous body increasingly shrinks due to some local or systemic disease, this may cause fissures or holes in the retina. Abnormal shrinking of the vitreous body is the most frequent cause of retinal detachment.

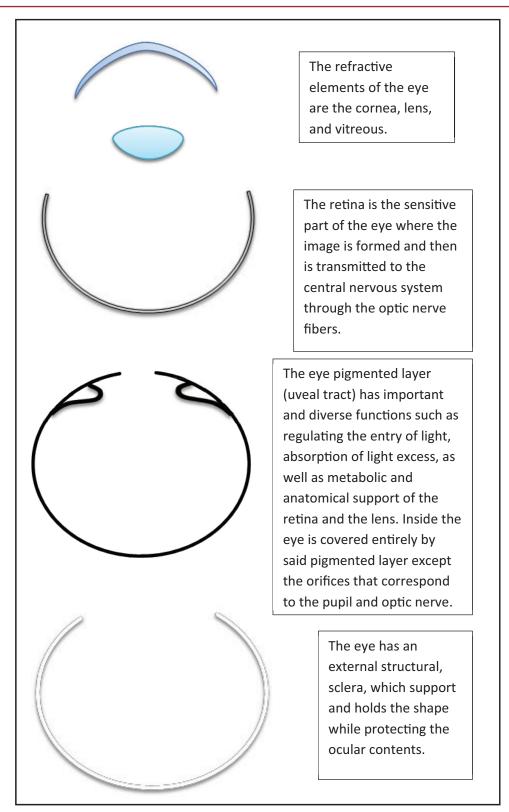


Figure 2: Outline of the main structures of the human eye. The pattern is notably similar in all species

RETINAL DETACHMENT

The risk of retinal detachment depends, among other factors, on the vitreous rheology, which varies with age. To date, the

viscoelasticity of the vitreous body has only been measured in cadaver eyes. Vitreous deformation during normal eye movements produces local vitreoretinal stresses^[5] which may, at some point, exceed the strength of retinal adhesion Vitreous body: Schematic representation of its gelatinous-like structure that occupies two-thirds to three-quarters of volume of adult eye (3.9 ml). The top notch corresponds to the space occupied by the lens and the lower groove to the optic nerve.



Figure 3: The vitreous body, which is located between lens and retina and consists of 98% of water, initially almost completely fills the eye, however, tend to lose fluid over time and correspondingly shrinks

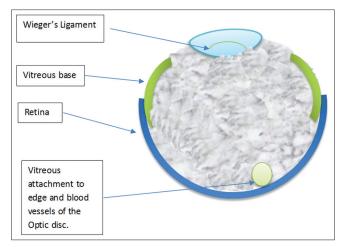


Figure 4: Vitreous attachments are vitreous base (green), posterior lens surface - Wieger's ligament - (green curved line); to the optic disk (pale green circle), also to the macula, equator, and retinal blood vessels. The retina is represented by the blue semicircle

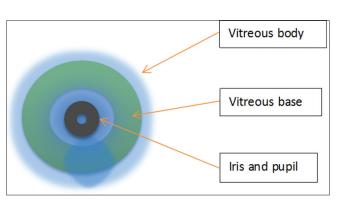


Figure 5: The vitreous base - anterior view - is represented by the green circle in a front view, approximate location. The blue color represents the total vitreous body viewed from the front



Figure 6: Usual appearance of vitreous when infiltrated with calcium compounds (white dots), the photograph was taken with a biomicroscope with a magnification of 16X



Figure 7: The same patient photographed with a magnification of 25X in the biomicroscope, Dx. Mineralization of the vitreous body

and cause retinal detachment, which is often observed in diseased eyes, with impaired adhesion mechanisms; but it is rarely observed in healthy eyes, this, with normal adhesion mechanisms [Figure 9-15].

MELANIN IS THE PIGMENT OF THE UVEAL TRACT

Melanin is a complex polymer pigment found in skin, hair, iris, ciliary body, and choroid, also in pigment epithelium of retina and iris, and in body obscure places as the dopaminergic neurons of the human substantia nigra, locus ceruleus, choroid plexuses, stria vascularis of inner ear, dura mater, etc.

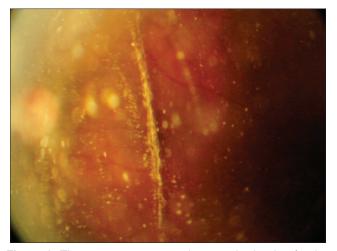


Figure 8: The same patient now photographed with a fundus camera where we can see, the left optic nerve (left side of photography) marred by vitreous opacities, retinal vessels at the back; and calcium compounds that extend even in the vitreous near to the retina. Calcium compounds tend to adhere to the collagen fibers of the vitreous

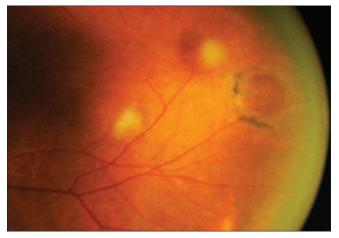


Figure 9: Vitreous body has a relevant role in ethiopathogeny of retinal tears. In this picture, a rounded retina fragment (upper right) has been torn, due to vitreous traction, leaving a circular hole (right) with partially pigmented borders

The structure of melanin is only partially characterized, and its synthesis pathway remains unknown.^[6]

Retinal, iris, and ciliary epithelial cells (all pigmented) are derived from neural ectoderm, in the distal end of the embryonic optical cup, which is also the origin of the retina.^[7] Oppositely, melanin-generating cells in the choroid and the stroma of iris and ciliary body (uveal melanocytes) are developed from the neural crest and the same origin as the melanocytes in the skin and hair.

The uvea (Lat. Uva, grape-color-) also called uveal tract, uveal coat, uveal layer, is a highly pigmented and vascularized



Figure 10: Ocular fundus photography of a patient with superior retinal detachment. The optic disc is seen as blurred orange circle (left). Retina detached is observed as a white veil in the upper part of the picture. Usually, the symptoms - perception of shadows, fog-like, smoke-like or grime like - are not accompanied by pain because the nerve fibers of the retina do not send pain information to the brain



Figure 11: The same patient of the anterior photography, but the optic disc is now focused. Anatomic details of the head of the optic nerve are now more visible. The optic nerve is seen behind the whitish retinal detachment

tissue that is located middle between retina and sclera. The iris, ciliary body, and choroid are the parts in which uveal tract is divided for study. The retina is supported anatomically by choroid; at least theoretically, choroid oncotic pressure is one of the forces that act pushing the retina against the retinal pigment epithelium (RPE).^[8]

The choroid layer of tissue is in intimate contact with the photoreceptors of the neural retina, called the RPE. RPE constitutes the major part of the metabolic support for the entire retina and is involved in phagocytosis of the photoreceptor outer segment, at rate of approximately one membranous disc per hour in a human being [Figures 9-14].

The RPE is contiguous with the iris pigment epithelium (IPE) and ciliary pigment epithelium (CPE) [Figure 17]. The melanin functions in these pigmented tissues are so far not fully



Figure 12: Once retinal tear is sealed through local inflammation induced surgically, the suction force of water dissociation of melanin now is able again to keep retinal tissue in the right place



Figure 13: Vitreous photographed through a biomicroscope in the live patient which corresponds to the same patient with retinal detachment [Figures 10 and 11], and thereby, collagen fibers have pathological features

elucidated. However, it has been observed that melanin has a protector role against several ocular diseases that can cause blindness, including age-related macular degeneration (AMD) and uveal melanoma. In patients with dark skin, AMD is very rare; however, in fair skin patients, AMD constitutes the first cause of blindness worldwide.

The exact mechanisms by which melanin protects the eye are presently unknown. Whether the protective function of melanin depends on the type of melanin (i.e., eumelanin or pheomelanin), cannot be answered because melanin formula is not known. Melanin hypothesized roles are linked to its interaction mainly with visible light; however, we must keep in mind that melanin is also able to interact with wavelengths that are invisible to the human eye.

The pigment epithelium of iris, ciliary body, and retina is densely pigmented in all races and in all eye colors. In regard, uveal melanocytes, quality, and quantity of melanin vary with race and skin and iris color. Human uveal melanocytes isolated and cultured *in vitro* produce melanin to maintain a constant level, but in human pigment epithelium cells the melanin production *in vivo*, or isolated and cultured conditions is uncertain.

Pigment epithelium cells form a wallpaper like into the eye and therefore is believed that aids in minimizing spurious signals that could appear because of light reflection and scatter from the fundus improving the quality of image formed. However, this melanin apparent photoscreen role cannot explain the protective effect of the higher melanin density in AMD or uveal melanoma [Figures 19 to 26].

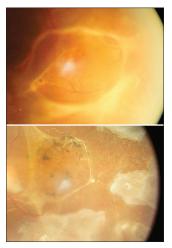


Figure 14: When vitreous body is abnormally shrunken, as happens in diabetes or trauma (above) characteristically has loss of elasticity and viscosity that normally is two to four times that of water, which changes its characteristics significantly and turning out into extreme rigidity that exerts abnormal traction on retinal tissue, and eventually detached it. The retina is able to recover its normal position when pathological vitreous body membranes are excised total or partially (bottom); thereby, the traction forces are relieved

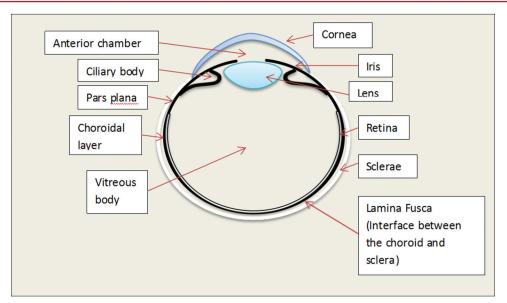


Figure 15: The eyeball and its main components are shown in this diagram. The uveal tract is drawn to dark brown and comprises the choroid, ciliary body, and iris

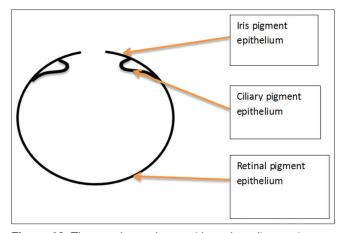


Figure 16: The uveal tract drawn without the adjacent tissues. The content of melanin is usually 40% more than in the skin. The pigmented ciliary epithelium is not in direct contact with the vitreous but in Bruch's membrane

NORMAL CHORIORETINAL ADHESION MECHANISMS

Ocular tissues are constantly exposed to acceleration and braking forces as result of the eye movements elicited by exteroceptive o interoceptive stimuli. All these eye movements are highly useful, and most of them are also reflex in nature, this is the individual is not aware that they are taking place, but they did not come about without the concurrence of attention. Eye performs with great accuracy saccadic and smooth movements in the service of the visual system, specifically in the interest of clear, distinct vision and binocular fixation. To give an idea of the magnitude of the forces generated during eye movements, we note that the average length of the extraocular muscles is 40 mm, cross-section $11-17.39 \text{ mm}^2$, their weight ranges from 0.51 to 0.75 g but seems disproportionate force, as for example, the medial rectus muscle is capable of moving a kg.^[10]

The eyeballs have intense and aleatory motion, in all directions, generating force vectors and complex moments with relatively strong forces, which would lead to tissue damage or even retinal detachment with relative ease, which, however, rarely occurs. The retina and RPE have different inertia, which causes friction between the components of either tissue, and it is remarkable that the anatomical and functional changes that might be expected from repeated micro-trauma are much smaller than one might think [Figure 19].

MOVEMENT OF THE VITREOUS BODY

The vitreous movement is important in the biology of the adhesion between the retina and RPE actor.

The volume of the adult vitreous body is slightly <3.9 ml, which are about two-thirds to three-fourths the volume of the adult globe. It is spherical posteriorly and saucer-shaped anteriorly, owing to the patellar fossa, a depression caused by the convexity of the posterior lens surface.

Anterior vitreous attachments

The vitreous body is attached anteriorly to the posterior lens surface by Wieger's ligament.

Herrera, et al.: Retinal detachtment and melanin

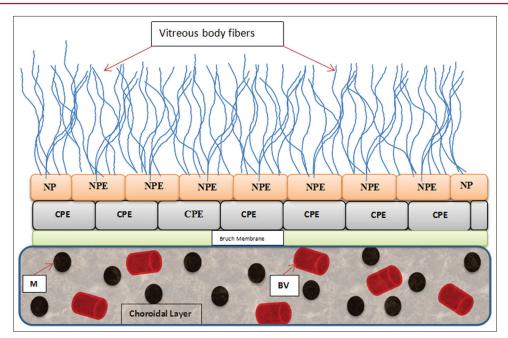


Figure 17: At the base of the vitreous body, in the anterior part of the eye, the collagen fibrils of the vitreous are strongly adhered to the cells of the unpigmented epithelium, and these, in turn; to the layer of pigmented epithelium. The Bruch membrane is considered as the basal membrane of the CPE. Externally, we have the choroid layer

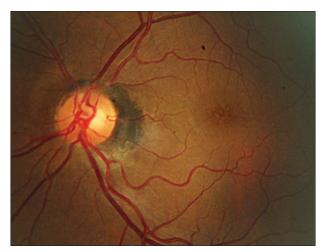


Figure 18: In this patient, melanin pigment is prominent in the temporal border of the optic disk, covering meridians from eleven to five

Vitreous base

In the region of the ora serrata, a firm adhesion exists between the vitreous cortex and the retina and pars plana ciliaris. This area of adhesion is termed the vitreous base. It is 2–3 mm wide and forms a circular band straddling the ora serrata and occupying approximately the posterior half of the pars plana ciliaris. Attempts to separate the vitreous body from its attachment at the vitreous base often result in some of the retina and epithelium of the pars plana ciliaris being torn of.

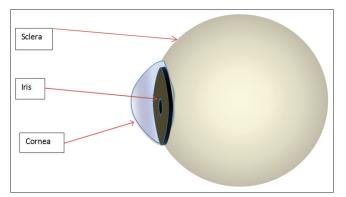


Figure 19: The sclera is a white tissue that completely covers the uvea, except the anterior portion which is transparent due to the cornea so just is possible to appreciate the coloration of the anterior portion of the uveal tract that is called iris. A side view diagram

The vitreous movement is a significant factor because it is a force that must be counteracted to maintain the normal position of the retina attached to the RPE.

THE WATER OF THE VITREOUS BODY

Both the retina and RPE offer a substantial resistance to water movement^[11] (Tsubai, 1987). Thereby, aqueous humor once is produced by ciliary processes and has an outward movement that, theoretically, pushes retinal tissue against

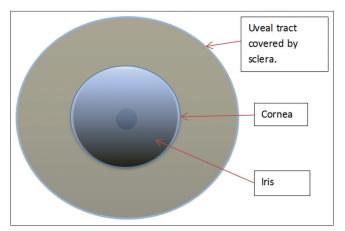


Figure 20: The sclera covers the uveal tract in almost all its extension. The uvea can be observed with its characteristic dark brown if we remove the sclera. Front view. Melanin behavior in response to environmental light intensity is congruous with the observed fact that greater amount of solar radiation causes a decrease in the incidence of uveal melanoma,^[9] an observed fact poorly understood



Figure 21: In the live patient, the choroidal melanin could be observed in some cases when tissues are slimed, as in this case of a patient with myopia

RPE. However, under normal conditions, there is a little posterior fluid flow in the eye [Figure 27].

THE MUCOPOLYSACCHARIDE MATRIX

The adhesive joint of the retina can be compared with an adhesive joint of two surfaces (RPE and photoreceptors) mediated by a thin layer of fluid viscous substance (the mucopolysaccharide matrix), but this simple model cannot explain the almost immediate retinal detachment in the dying body nor the rarity of retinal detachment among dark skin people.^[12]

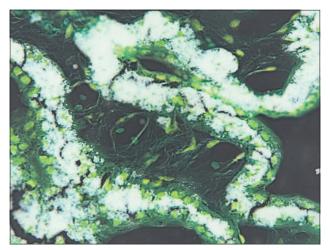


Figure 22: Approximation of the levels of free chemical energy in a histological section of a Wistar rat ciliary process stained with hematoxylin and eosin and then processed digitally. Cell nuclei were seen prominent in light green, indicating an important metabolic activity. Melanin is seen white (highest free chemical energy levels). Ciliary processes are covered by two monolayers of cuboidal cells, the most pigmented layer is in contact with the stroma of ciliary body, and the less pigmented layer is the closest to the vitreous body

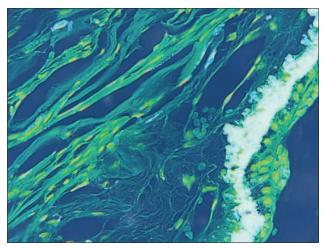


Figure 23: Approximate levels of free chemical energy in Wistar rat ciliary body section. The longitudinal muscle fibers (top left) show its elongated nucleus in bright green color and the presence of loose connective tissue. Near the center of the picture, a stack of erythrocytes was seen (green). To the right of the photograph, melanin (white) is contained inside the pigmented epithelium of the ciliary body (CBPE), and a monolayer of non-pigmented epithelium is observed on the CBPE being considered as an extension of the retinal tissue that extends from the ora serrata to pupillary edge of the iris. If we interpret the white color of the melanin as a zone of maximum level of free chemical energy, the oval yellowish structures, corresponding to cells nuclei, suggest a significant metabolic activity, and on the other hand, the erythrocytes (darkest green) indicates less metabolic activity than the nucleated cells

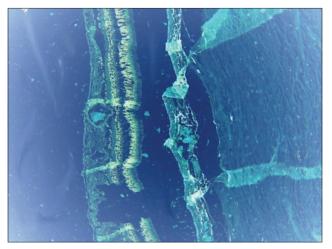


Figure 24: In this histological section are shown, the retina (left), sclera (right), and in the middle part of the choroid. The separation of the retina from the RPE is the rule in histological studies

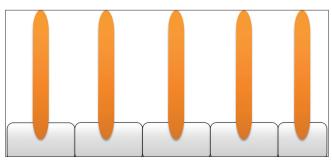


Figure 25: Schematic representation of the photoreceptors (orange) that intertwined with the cells of the RPE (gray), which in turn are settled, as any epithelium; on a basement membrane called Bruch's membrane (green)

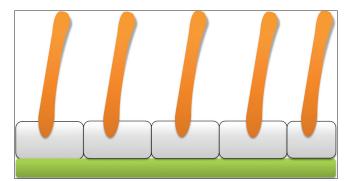


Figure 26: Intense movement of the eyeball, both during wakefulness and during sleep, causing friction between the different layers of the eye, given the different inertias of the various tissues that make up; causing wear and eventually breakage of structures over time, which would be greater if not for the flexibility that is, in the case of the union of the photoreceptors with the pigmented epithelium of the retina; which can lean to one side or the other, reducing the traction between the different structures; as photoreceptors and RPE cells are joined together by Velcro mechanism-like manner

It is a well-known fact that vitreous traction can disrupt retinal adhesion in life, but that retinal detachment is the rule in the dead body which indicates that the adhesion between the retina and RPE is a dynamic process, i.e., it requires energy expenditure. For a long time, researchers have reported that it is more difficult to induce retinal detachment in experimental animals in light than under dark conditions.^[13]

The adhesive strength of the pigment epithelium elements increases 2–3 times after light adaptation in the live specimen, but, within a few minutes of death, fades quickly. Therefore, retinal adhesion *in vivo* is stronger than shortly after dead [Figure 28].

The adhesion of the neural retina to the RPE is essential to the metabolism of photoreceptors and the process of vision. A definite anatomical attachment between these two layers has not been demonstrated. Their contact is mediated by an amorphous matrix of mucopolysaccharides and projection of the distal end of the photoreceptors (finger processes-like) in RPE cells, which results in a depression in the anatomy of RPE cells, but without any known type of anatomical adhesion formation [Figure 29].

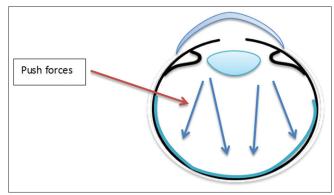


Figure 27: The push forces that result from posterior flow of aqueous humor are more theoretical than real

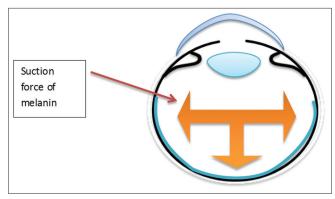


Figure 28: The vacuum-producing melanin is mainly generated along the uveal tract, resulting that surrounding tissues (retina) are attracted to it. This means that the normal position of the retina requires constant energy output, day and night

Comparison of the traction *in vivo* with traction postmortem has indicated the presence of an additional force which enhances the adhesion in the living animal.^[14] The nature of this force has been a matter of speculation for long time, but metabolic exchanges occurring at the retina-pigment epithelium interface and possible pressure gradient across the retina are the most mentioned.

It has been clearly shown that there is a significant difference in the mechanism of retinal adhesion *in vivo* as opposed to that in enucleated eyes.

On the other hand, the adhesion of the retina to the pigment epithelium seems stronger at the equator than at the posterior pole.

THE ROLE OF MELANIN IN OCULAR PHYSIOLOGY AND PATHOLOGY

Melanin functions already described are only as photoscreen, a weak free radical scavenger, and antioxidant.^[15] Melanin light absorption capacities on diverse wavelengths^[16] supposedly diminished detrimental effects of ultraviolet (UV) radiation that is a cause of cellular gene mutation that leads to malignant mutation of uveal melanocytes. Reactive oxygen species (ROS), both UV induced and biochemically produced, also play a role in the degeneration of photoreceptors of neural retina.

The lower incidence of macular degeneration and retinal detachment in dark pigmented eyes reported in the literature, it is explained (wrongly) as related to the lesser light intensity that is transmitted to the retina. Paradoxically, it has been reported that increases in solar radiation cause a decreases in

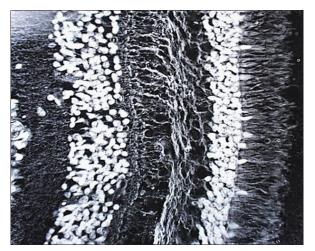


Figure 29: Histological section of human retina stained with hematoxylin and eosin and then processed digitally. To the right, we have the photoreceptors (rods and cones) layer that is in direct contact with RPE cells (not visible in this photography) 100X

the incidence of uveal melanoma (Hu *et al.*, 2008). Recently, it has been reported that solar radiation reduces the risk and/ or mortality of various systemic malignant tumors that are no exposed to sunlight, that is, non-Hodgkin lymphoma, prostate, breast, colon, and ovarian cancers. Thereby, sunlight has a dual effect on tissues exposed to the sunlight and an indirect protective effect on tissues not exposed to sunlight.^[17] Sunlight dual effects on tissues exposed and not exposed to sunlight have been explained in basis that UV radiation increases Vitamin D synthesis in the skin.

Theoretically, melanin may deactivate ROS and protect the retina from oxidative damage. However, with age, the constant and frequent exposure of pigment cells to high levels of oxygen may diminish the antioxidant properties of melanin, and eventually, melanin may become a pro-oxidant which sooner or later may cause damage to photoreceptors. Therefore, eyes with dark-colored irides contain a greater amount of melanin and therefore can resist ROS and protect better and longer time the retinal tissues.

THE INTRINSIC PROPERTY OF MELANIN TO TRANSFORM LIGHT ENERGY INTO CHEMICAL ENERGY

Melanin is a pigment that has drawn attention for centuries. However, it is almost impossible to study in isolation in the laboratory, which impeded progress in the knowledge of their true function in the eye and in the human body. It was not until the 1990s, when during a descriptive study of the anatomical changes in the optic nerve vasculature accompanying the three leading causes of blindness in the world - glaucoma, diabetes, and degeneration macular - we identify its unexpected ability to transform light energy into chemical energy through the dissociation of the water molecule in a similar way as it does chlorophyll. The reaction that happens into the chlorophyll can be written as follows:

 $2H_2O$ (liquid) $\rightarrow 2H_{2(gas)} + O_{2(gas)}$

Moreover, melanin, the dissociation of the water molecule occurs in almost identical form:

 $2H_2O$ (liquid) $\leftrightarrow 2H_{2(gas)} + O_{2(gas)} + 4e^{-1}$

However, the differences are crucial, since the chlorophyll reaction is irreversible, and melanin, happens both dissociation and re-association of the water molecule. For each two molecules of water reformed, four high-energy electrons are obtained. Furthermore, chlorophyll is only able to absorb energy near the ends of visible light, namely blue and red, but the melanin is able to absorb the entire visible spectrum and even beyond.^[18]

Plants and humans seems to follow the concept: "Hydrogen, like any other energy carrier it must be produced from a *primary energy source*, "^[19] and in this case, the primary source of energy is sunshine, specifically visible light extremes; this is red and blue in the case of chlorophyll and the full electromagnetic spectrum in the case of melanin.

Emanating chemical energy is released by melanin symmetrically in all directions in the form of growing spheres. [Figure 30].

The real value product of dissociation of water molecule is diatomic hydrogen as is the carrier of energy for excellence in the entire universe. Molecular hydrogen has the important characteristic of not combine with water, allowing it to diffuse through the cytoplasm of the cell carrying their precious cargo of energy every corner, and along the way, he is eventually captured by the cellular organelles, who use energy in many ways, including up to retain the shape. Thereby, glucose is just a source of carbon chains, of biomass at most; however, the

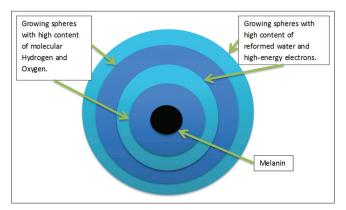


Figure 30: The growing fields of energy released by melanin would be alternating nature, namely a higher proportion contain hydrogen and molecular oxygen, and the next would have a greater proportion of reformed water and high energy electrons



Figure 31: Polyethylene teraphthalate (PET) bottle with drinking water and melanin impregnated in silicum (bottom). After few days, PET bottle deformation is evident

main source of energy of eukaryotic cell is water, both plants and humans. If we tried to replace the energy of light with energy from food, would have to eat about 180 kg every 24 h.

The strategic location of melanin granules in the perinuclear space allows the free chemical energy emanating from the melanin in the form of diatomic hydrogen and high energy electrons, reaching every corner of the cell, which constitutes entirely the energetic supply of the cell. It is important to remember that 75% of the known universe consists of hydrogen, on the other hand, is the ultimate energy carrier, also in the entire universe; and finally, diatomic hydrogen is the best antioxidant known so that several functions are carried out and all are important.

Glucose provides carbon, hydrogen and oxygen to the organism in the form of a soluble structure, which are used for the synthesis of 99% of the biomolecules that make up us. However, energy, defined as anything that produces a change, making our body water, like plants.

The unexpected discovery of the body's ability to capture the light energy through the dissociation of the water molecule, such as plants, leads to radically change the old concept



Figure 32: The PET bottle on the left contains the impregnated melanin (bottom) and the right bottle is also PET and also contains water but not containing melanin. The differences between both front and profile are undeniable and very significant

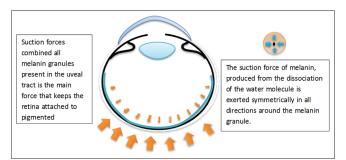


Figure 33: The amount of melanin present in the uveal body generates a vacuum of sufficient magnitude to maintain ocular tissues in suitable location and functions. The vacuum draws not only the retina but also other tissues, for example, the sclera; as well as orbital and intraocular fluids, which are carried out by the bloodstream, as part of its cycle

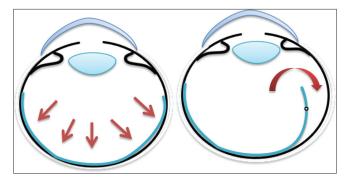


Figure 34: When the retina has no tears or holes (left), the vacuum that produces melanin exerts a suction force, suitable on the retinal tissue, which keeps it in place, i.e., in the normal close contact with the RPE. However, when an injury occurs, a hole or tear is formed on the retina (right), then the suction force decreases significantly because fluids, attracted by the suction of melanin, quickly begin to enter into the subretinal space through the tear itself, following the path with fewer obstacles, which maintains and even increases the separation of the RPE of the retina, which induces a rapid degeneration of the rods and cones, with consequent loss of vision, that in matter of few days is irreversible

that our body which is made up of trillions of energetically dependent cells for in reality each cell is capable of generating its own energy through dissociation of the water molecule, so on the basis that, we really are formed by energetically independent cells; it is necessary to rethink the metabolism as a whole, which is beyond the purpose of this article; therefore, we will refer only to the function of melanin in relation to retinal adhesion mechanisms.

THE ROLE OF MELANIN IN THE MECHANISMS OF ADHESION OF THE RETINA

The unsuspected intrinsic property of melanin to split the water molecule^[20] is a surprising finding that breaks the ground because it changes dramatically the traditional role of melanin in ocular tissues. The puzzle about why the retina is held in place while the subject is alive and separated from the RPE within minutes after death is solved by considering the intrinsic property of melanin to transform light energy into chemical energy. Moreover, the explanation is surprisingly simple: The continuum of dissociation and reformed from the water molecule, in addition to providing chemical energy that is essential to drive and control each one of intracellular biochemical processes, generates a vacuum [Figure 28], which is demonstrable through relatively simple experiments.

Melanin impregnated silica was placed in a water bottle of flexible plastic and a bottle of similar characteristics but without the melanin, before long, flexible bottle containing melanin deforms significantly [Figures 31-33].

When we introduce a latex balloon in the mouth and aspire, latex copies the anatomy of the mouth, but if we drilled the balloon, then it does not happen. Something similar happens with the retina, where the suction force that produces melanin, keeps the retina in place, but if the retinal tissue has a tear or hole, then the retina detaches [Figure 34].

Retinal detachment impairs severely photoreceptor layer. Rods and cones, when lose close contact with the pigmented epithelium of the retina, in matter of hours, show significant degenerative changes that are rapidly progressive and with consequent loss of visual function.

CONCLUSION

Before the discovery of the intrinsic property of the melanin to transform light energy into chemical energy available in intracellular milieu through dissociation of the water molecule, the normal position of the retina, in close contact with PER, that is observed only in the living patient, had not been satisfactorily explained. The fact that the retina is detached almost immediately after death, indicating that it is a dynamic process, e.g., requires energy expenditure; so far is traditionally attributed to the intraocular pressure and the oncotic pressure of the blood flow in the choroid. However, elevated intraocular pressure (Glaucoma) does not prevent retinal detachment, and vitreous oncotic pressure is zero.

The unexpected ability of melanin to dissociate and reform the water molecule satisfactorily explains the adhesion of the retina to the RPE because on one hand generates the necessary chemical energy to maintain the dynamics of the process, and second, a suction force is generated by the constant dissociation and reforming the water molecule.

ACKNOWLEDGMENT

This work was supported by an unrestricted grant of Human Photosynthesis® Research Center.

REFERENCES

- 1. Howland HC, Merola S, Basarab JR. The allometry and scaling of the size of vertebrate eyes. Vision Res 2004;44:2043-65.
- Fine BS. Retinal structure: Light and electron microscopic observations. In: McPherson A, editor. New and Controversial Aspects of Retinal Detachment. New York: Harper and Row, Publishers; 1968. p. 15-62.
- François J, Victoria-Troncoso V, Albarran E. The histiochemical structure of the vitreous fibers studies by phase contrast microscopy. Am J Ophthalmol 1970;69:763-73.
- Foos RY. Vitreoretinal juncture; Topographical variations. Invest Ophthalmol 1972;11:801-8.
- 5. Piccirelli M, Bergamin O, Landau K, Boesiger P, Luechinger R. Vitreous deformation during eye movement. NMR Biomed

2012;25:59-66.

- Liu Y, Hong L, Wakamatsu K, Ito S, Adhyaru BB, Cheng CY, et al. Comparisons of the structural and chemical properties of melanosomes isolated from retinal pigment epithelium, iris and choroid of newborn and mature bovine eyes. Photochem Photobiol 2005;81:510-6.
- Hu DN, Simon JD, Sarna T. Role of ocular melanin in ophthalmic physiology and pathology. Photochem Photobiol 2008;84:639-44.
- Kita M, Marmor MF. Effects on retinal adhesive force *in vivo* of metabolically active agents in the subretinal space. Invest Ophthalmol Vis Sci 1992;33:1883-7.
- 9. Hu DN, McCormick SA, Yu GP. Latitude and uveal melanoma. Ophthalmology 2008;115:757.
- Hermann MB, Gunter KV. Summary of the gross anatomy of the extraocular muscles. In: Binocular Vision and Ocular Motility. Ch. 3. Saint Louis: The C.V. Mosby Company; 1974. p. 44-53.
- 11. Tsuboi S. Measurement of the volume flow and hydraulic conductivity across the isolated dog retinal pigment epithelium. Invest Ophthalmol Vis Sci 1987;28:1776-82.
- Hanan Z. Normal chorioretinal adhesion. In: Pruett RC, Regan CD, editors. Retina Congress. Ch. 49. New York: Appleton-Century Crofts; 1972. p. 573-81.
- Zauberman H, Berman ER. Measurement of adhesive forces between the sensory retina and the pigment epithelium. Exp Eye Res 1969;8:276-83.
- 14. Zauberman H, DeGuillebon H. Retinal traction in vivo and

postmortem. Arch Ophthalmol 1972;87:549-54.

- 15. Hu DN, Savage HE, Roberts JE. Uveal melanocytes, ocular pigment epithelium, and müller cells in culture: *In vitro* toxicology. Int J Toxicol 2002;21:465-72.
- Sarna T, Swartz HA. The physical properties of melanin. In: Nordlund JJ, Boissy RE, Hearing VJ, King RA, Ortonne JP, editors. The Pigment System, Physisiology and Pathophysiology. Oxford: Oxford University Press; 1998. p. 333-58.
- Zareba M, Raciti MW, Henry MM, Sarna T, Burke JM. Oxidative stress in ARPE-19 cultures: Do melanosomes confer cytoprotection? Free Radic Biol Med 2006;40:87-100.
- Solis-Herrera A, Arias-Esparza MC, Solís-Arias RI, Solís-Arias PE, Solís-Arias MP. The unexpected capacity of melanin to dissociate the water molecule fills the gap between the life before and after ATP. Biomed Res 2010;21:224-6.
- Royal Belgian Academy Council of Applied Science: Hydrogen as an Energy Carrier; 2006. Available from: https://www. sciencedirect.com/science/article/pii/S0360319916318109. [Last accessed on 2014 Nov 14].
- Solís-Herrera A, Arias-Esparza MC, Solis-Arias MP. Energy production, the main role of melanin in the mesencephalon. J Appl Med Sci 2013;2:11-20.

How to cite this article: Herrera AS, Esparza MCA, Arias PES. The role of melanin in retina detachment. Clin Res Ophthalmol 2018;1(2):1-14.