Molecular Aspects of Medicine 33 (2012) 295–317

Contents lists available at SciVerse ScienceDirect

Molecular Aspects of Medicine

journal homepage: www.elsevier.com/locate/mam

Review

Understanding age-related macular degeneration (AMD): Relationships between the photoreceptor/retinal pigment epithelium/Bruch's membrane/choriocapillaris complex

Imran Bhutto, Gerard Lutty *

Wilmer Ophthalmological Institute, Johns Hopkins Hospital, Baltimore, MD, United States

ARTICLE INFO

Article history:
Available online 21 April 2012

Keywords:
Age-related macular degeneration
Bruch's membrane
Choriocapillaris
Retinal pigment epithelium
Photoreceptors

ABSTRACT

There is a mutualistic symbiotic relationship between the components of the photoreceptor/retinal pigment epithelium (RPE)/Bruch's membrane (BrMb)/choriocapillaris (CC) complex that is lost in AMD. Which component in the photoreceptor/RPE/BrMb/CC complex is affected first appears to depend on the type of AMD. In atrophic AMD (~85–90% of cases), it appears that large confluent drusen formation and hyperpigmentation (presumably dysfunction in RPE) are the initial insult and the resorption of these drusen and loss of RPE (hypopigmentation) can be predictive for progression of geographic atrophy (GA). The death and dysfunction of photoreceptors and CC appear to be secondary events to loss in RPE.

In neovascular AMD (~10–15% of cases), the loss of choroidal vasculature may be the initial insult to the complex. Loss of CC with an intact RPE monolayer in wet AMD has been observed. This may be due to reduction in blood supply because of large vessel stenosis. Furthermore, the environment of the CC, basement membrane and intercapillary septa, is a proinflammatory milieu with accumulation of complement components as well as proinflammatory molecules like CRP during AMD. In this toxic milieu, CC die or become dysfunction making adjacent RPE hypoxic. These hypoxic cells then produce angiogenic substances like VEGF that stimulate growth of new vessels from CC, resulting in choroidal neovascularization (CNV). The loss of CC might also be a stimulus for drusen formation since the disposal system for retinal debris and exocytosed material from RPE would be limited. Ultimately, the photoreceptors die of lack of nutrients, leakage of serum components from the neovascularization, and scar formation.

Therefore, the mutualistic symbiotic relationship within the photoreceptor/RPE/BrMb/CC complex is lost in both forms of AMD. Loss of this functionally integrated relationship results in death and dysfunction of all of the components in the complex.

© 2012 Elsevier Ltd. All rights reserved.

Contents

* Corresponding author. Address: G. Edward and G. Britton Durell Professor of Ophthalmology, Wilmer Ophthalmological Institute, M041 Smith Building, 400 North Broadway, Johns Hopkins Hospital, Baltimore, MD 21287-9115, United States. Tel.: +1 410 955 6750; fax: +1 410 955 3447.
E-mail address: Glutty1@jhmi.edu (G. Lutty).

0098-2997/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.mam.2012.04.005

1. Basic normal anatomy of the photoreceptor/retinal pigment epithelium (RPE)/Bruch's membrane (BrMb)/ choriocapillaris (CC) complex

The components of the photoreceptor/retinal pigment epithelium (RPE)/Bruch's membrane (BrMb)/choriocapillaris (CC) complex have a mutualistic symbiotic relationship (Fig. 1). Each is dependent on the other components in the complex and each contributes to the well being of the others. We will first discuss each component in the complex in healthy human eyes and then discuss how each is changed in age-related macular degeneration. Finally, we will consider the breakdown of the mutualistic symbiotic relationship in AMD.

1.1. Photoreceptors

The photoreceptors are a specialized type of neuron in the posterior retina that are capable of phototransduction. Photoreceptors convert light into signals that can stimulate neuronal impulse transmission by triggering a change in the cell membrane potential after absorbing a photon. The two classes of photoreceptor cells are rods and cones and the signal they generate are converted to vision. The rods are narrower than the cones and distributed differently across the retina, but the chemical process in each that supports phototransduction is similar. However, rods are extremely sensitive and can be triggered by a very small number of photons. At very low light levels, visual experience is calculated solely from the rod signal. Cones require significantly brighter light in order to produce a signal. In humans, there are three different types of cone cells (red, green blue), distinguished by their pattern of response to different wavelengths of light. The human anatomical macula is only 6 mm in diameter and it contains a small cone dominated fovea (0.8 mm) (Fig. 1) surrounded by a rod-dominated parafovea (Curcio et al., 1996, 1990; Curcio, 2001). It is estimated by Curcio that only two rods/mm^2 of retina die per year. Barron and associates found mitochondrial DNA deletions and cytochrome c oxidase-deficient cones accumulate in the aging retina, particularly in the foveal region. These defects may contribute to the changes in macular function observed in aging and age-related maculopathy (Barron et al., 2001).

The photoreceptor inner segments are rich in mitochondria, which are needed to provide energy for these highly metabolically active cells. The photoreceptors consume more oxygen per gram of tissue weight than any cell in body and have a tissue oxygen level close to zero in the dark (Wangsa-Wirawan and Linsenmeier, 2003).

1.2. Retinal pigment epithelium (RPE)

Just posterior to the photoreceptors, the RPE are polarized epithelial cells found at the base of the retina. The RPE consists of a single layer of hexagonal cells that are densely packed with pigment granules (melanosomes). The RPE are firmly attached to their underlying basement membrane, which is the inner or anterior layer of Bruch's membrane. At the ora serrata, the RPE continues as a membrane passing over the ciliary body and continuing as the posterior surface of the iris. At its apical surface of the RPE faces the photoreceptor outer segments making a complex of close structural interactions. With its basolateral surface, the RPE faces Bruch's membrane (BrMb), which separates the RPE from fenestrated endothelium of the choriocapillaris (CC). When viewed in cross section, each RPE cell consists of a basal outer non-pigmented part containing a large oval nucleus and an anterior-pigmented portion, which extends as a series of finger-like processes between the photoreceptor outer segments.

Download English Version:

https://daneshyari.com/en/article/1995836

Download Persian Version:

https://daneshyari.com/article/1995836

Daneshyari.com