The Retinal Pigment Epithelium of Wild Type (C57BL/6J +/+ ) and Pearl Mutant (C57BL/6J pe/pe) Mice

Marilyn A. Williams, Lawrence H. Pinto, and Janine Gherson

The retinal pigment epithelium (RPE) lying along the vertical meridian of the eyes of wild-type (+/+ ) and pearl mutant (pe/pe) mice was examined with electron microscopy and microspectrophotometry in order to compare differences in melanosome location, size, numerical density, volume density, and melanin concentration. In +/+ mice the fraction of melanosomes that lie in the apical processes was greater in the superior than in the inferior retina. Also, the numerical density and volume density of soma melanosomes were lower in the superior retina. The soma melanosomes were also located closer to the basal membrane and had a larger average diameter in the inferior retina. No significant differences in melanosome location were observed between light-adapted and dark-adapted retinas. In pe/pe mice the fraction of melanosomes in the apical processes was very low in both inferior and superior retinas. The numerical density and the volume density of soma melanosomes of pe/pe were significantly less than those of +/+ . The soma melanosomes of pe/pe mice lie closer to the basal membrane than those of +/+ , and they had a larger mean diameter than those of +/+ . Electron micrographs depicted some melanosomes of pe/pe with irregular profiles and abnormal melanin deposition at their periphery. Microspectrophotometric measurements of individual melanosomes in semithin sections showed that maximal specific absorption and \( \lambda_{\text{max}} \), were nearly equal for both genotypes and both superior/inferior locations. These findings show that intramelanosomal melanin concentration is normal for pe/pe. The basal membrane of the RPE of pe/pe was infolded over only 80% of the area covered by the basal surface, whereas the basal membrane in +/+ was infolded over more than 98% of the area covered. The boundary density of RPE basal infoldings was also lower in pe/pe than in +/+ . Furthermore, some areas of the basal lamina of pe/pe RPE had a periodic, rather than an amorphous, structure. These findings suggest that the reduced retinal sensitivity found in intact pe/pe animals, but not in superfused, isolated pe/pe retinas, may result from impaired transport of a diffusible substance by the basal membrane of the RPE. Invest Ophthalmol Vis Sci 26:657-669, 1985

Pearl mutant mice have several visual abnormalities that may be related to defects in their retinal pigment epithelia. First, certain retinofugal projections are altered or reduced and such changes have been shown to be a property of animals with abnormally pigmented retinal pigment epithelia (see LaVail et al for studies in the mouse). Second, sensitivity, measured using retinal ganglion cell responses, is reduced in the intact, anesthetized preparation, but not in the isolated, superfused retina (from which the pigment epithelium is removed). In addition, pearl rod terminals, in light-adapted eyes fixed in situ, exhibit some synaptic lamellae with bulbous thickenings or adjacent electron-dense bodies. However, isolated retinas rarely exhibit such modified synaptic lamellae following light adaptation in vitro (unpublished observations). Hence, in the absence of the PRE, retinal function and photoreceptor synaptic morphology are normal.

For these reasons we studied the ultrastructural composition of the pigment epithelium of wild-type and pearl mice in order to search for defects that might help us to understand the altered structure and function of the pearl retina. Our findings indicate low numbers and abnormal size and location of melanosomes, and a reduced area of the basal pigment epithelial membrane in pearl mice. These results have been reported in brief previously.

Materials and Methods

Fourteen wild-type mice from the C57BL/6J strain and 16 congenic pearl (C57BL/6J pe/pe) mice, aged 2–10 months in both groups, were anesthetized with ether, and perfused intracardially with a formaldehyde–glutaraldehyde mixture. Four to 24 hours later the eyes were removed and bisected along the vertical meridian, and the superior cornea was marked. The

From the Department of Biological Sciences, Purdue University, West Lafayette, Indiana.

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Reprint requests: Marilyn A. Williams, PhD, Department of Biological Sciences, Purdue University, West Lafayette, IN 47907.
eyes were then processed for electron microscopy as described. 7

The mice were maintained on a 12-hr light/12-hr dark cycle, with the light period beginning at 0700. Perfusion were done between 1100 and 1500. Dark-adapted retinas were obtained from animals that had been kept in total darkness for either 3 or 15 hr before perfusion, and were perfused with the aid of infrared illumination and an infrared-sensitive television camera. All procedures involving mice were performed in concordance with the ARVO Resolution on the Use of Animals in Research.

Melanosomes, the most electron-dense organelles in the cytoplasm, were distinguished from lipofuscin granules, which were distinctly less electron-dense. Melanolipofuscin granules exhibited regions of high density and regions of moderate density reflecting the dual composition of these organelles. Ultra-thin sections of pearl retina containing irregularly shaped melanosomes (see Results) were oxidized with 10% hydrogen peroxide in order to verify that these organelles contained melanin. The hydrogen peroxide treatment bleached all melanosomes but not the lipofuscin granules.

Quantification of melanosome size and location was made in transverse sections of the RPE in regions 0.25–0.75 mm from the head of the optic nerve. Mosaic photomicrographs (×10,000) of the region to be studied were made, and the apical melanosomes and melanosomes of smallest detectable diameter were marked (Fig. 1). The minimum diameter of each melanosome, the distance of each melanosome from the basal membrane, and the thickness of the pigment epithelial cells (in each individual micrograph) were measured using a digital graphics tablet. The distribution of melanosome diameter was calculated using the Coupland correction for non-centered sections 8 and the Abercrombie correction 9 with the Floderus modification 10 for section thickness, which was taken as 0.1 μm in all cases where thickness could not be measured using the "Small fold" technique (see Weibel 11 p. 148). Numerical density was
calculated as the ratio of the corrected total number of melanosomes to the volume of pigment epithelial cell soma in which the melanosomes were found. We did not attempt to quantify the size of the apical melanosomes because their profiles varied greatly from animal to animal, owing to variations in the cutting angle with respect to their long axes. The distance of the melanosome from the basal lamina of the pigment epithelial cell (a in Fig. 1) was normalized with respect to mean thickness of the cell, excluding apical processes (b, the mean of at least 8 measurements such as b in Fig. 1) to yield a
Fig. 4. Distribution of diameters of soma melanosomes of RPE cells from superior and inferior retinas of light-adapted C57BL/6J +/+ mice.

Table 1. Comparison of melanosome properties in superior and inferior retinas of wild-type mice; the melanosomes of the inferior retina are more abundant, larger, and less likely to be located in the apical processes than those in the superior retina. Melanosomes in the apical processes of the inferior retina are located nearer to the cell body.

<table>
<thead>
<tr>
<th>Region of retina</th>
<th>State of adaptation</th>
<th>Melanosomes counted</th>
<th>Density of all melanosomes (uncorrected)</th>
<th>% Apical melanosomes (uncorrected)</th>
<th>Average location of apical melanosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior retina</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior retina</td>
<td>Light</td>
<td>13 ± 2</td>
<td>12 ± 2</td>
<td>1.13 ± 0.40</td>
<td>1.10 ± 0.35</td>
</tr>
<tr>
<td></td>
<td>Dark</td>
<td>31 ± 2</td>
<td>28 ± 7</td>
<td>1.26 ± 0.49</td>
<td>1.21 ± 0.44</td>
</tr>
<tr>
<td>Total no. of melanosomes counted</td>
<td>3051</td>
<td>5880</td>
<td>1926</td>
<td>1293</td>
<td>354</td>
</tr>
</tbody>
</table>

Location of melanosomes expressed as f, whose value is 0 at the basal membrane and 1.0 at the apical membrane (see Materials and Methods). Mean ± SEM values are given.  
† See Figure 5A.  
‡ See Figure 5B.  
§ See Figure 4.

Table 2. Comparison of melanosome properties of pearl mutant and wild-type retinas; the pearl retina shows very few apical melanosomes, and those in the soma are larger, less abundant, and closer to the basal membrane than those of wild-type.

<table>
<thead>
<tr>
<th>Region of retina</th>
<th>State of adaptation</th>
<th>Melanosomes measured</th>
<th>% Apical melanosomes (uncorrected)</th>
<th>Average location of soma melanosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild-type</td>
<td></td>
<td></td>
<td>13 ± 1.9</td>
<td>0.65 ± 0.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12 ± 1.9</td>
<td>0.66 ± 0.63</td>
</tr>
<tr>
<td>Wild-type</td>
<td></td>
<td></td>
<td>31 ± 2.2</td>
<td>0.49 ± 0.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>28 ± 6.5</td>
<td>0.47 ± 0.58</td>
</tr>
<tr>
<td>Pearl</td>
<td></td>
<td></td>
<td>0.7 ± 0.42</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.0 ± 0.42</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.9 ± 1.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.6 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>Region of retina</td>
<td>Inf</td>
<td>3658</td>
<td>1726</td>
<td>3417</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1269</td>
<td>1590</td>
</tr>
</tbody>
</table>

Location of melanosomes is expressed as f, whose value is 0 at the basal membrane and 1.0 at the apical membrane (see Materials and Methods). Mean ± SEM values are given. Inf: inferior; sup: superior.  
† See Figure 9.
the lines of the test system (total length, l) were counted. Boundary length density was determined using the formula \( B_A = \frac{\pi}{2} l/l \). The test system was placed over electron micrographs (×26,000) from 10 to 14 locations of the basal infolding area to yield data from 10 to 14 retinal pigment epithelial cells per eye. A length of about 200–300 \( \mu m \) (referred to the eye) of test grid lines for each eye was counted in order to obtain an expected probable error of less than 5% for each measurement (Weibel, p. 119) from four wild-type mice and three pearl mutant mice.

Microspectrophotometric measurements of melanosome specific absorption (the absorption per thickness of tissue traversed by the measuring light) were performed upon sections 0.2–0.8 \( \mu m \) thick (chosen to give melanosome absorbance of 0.2–0.5) that had received neither osmium tetroxide nor uranyl acetate treatment. Sections were mounted on glass microscope slides, and section thickness was measured with a Jamin-Lebedeff interference microscope before applying a coverslip. The unstained sections were then photographed, and the largest, most fully melanized melanosomes were chosen for measurement using the method of Griff and Pinto. An oil-immersion condenser [1.4 numerical aperture (NA)] and objective (1.4 NA) were used to illuminate a melanosome and cast its image onto the mask of a photometer that could be moved in the image plane. We found the stability of focus better if we warmed the immersion oil to body temperature prior to its application. A wheel that rotated once per second and carried six interference filters allowed data to be collected for the six wavelengths rapidly and in an interleaved fashion to minimize drift. The photomultiplier tube (PMT) was a Hamamatsu R936 (Hamamatsu City, Japan), and supplementary neutral density filters were placed with each interference filter to evoke nearly equal output currents from the PMT. A rotating microscope nosepiece was used with an iris and various pinholes to alter the photometer mask size, and alignment of the chosen melanosome with the measuring pinhole (which was smaller than the melanosome image) was aided by placing an illuminated graticle in the eyepiece. The melanosome specific absorption spectra were computed from differences between the absorption spectra obtained with light traversing the melanosome and light traversing an immediately adjacent region; the difference spectra

<table>
<thead>
<tr>
<th>Average location of soma melanosomes</th>
<th>Corrected average diameter of soma melanosomes (( \mu m ))</th>
<th>Corrected numerical density of soma melanosomes (( \mu m^{-3} ))</th>
<th>Volume density of soma melanosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light &amp; Light§</td>
<td>0.66 ± 0.63</td>
<td>0.71 ± 0.66</td>
<td>0.53 ± 0.03</td>
</tr>
<tr>
<td>Dark &amp; Dark§</td>
<td>0.66 ± 0.63</td>
<td>0.71 ± 0.66</td>
<td>0.48 ± 0.04</td>
</tr>
<tr>
<td>3290 &amp; 3804</td>
<td>0.40 ± 0.76</td>
<td>0.32 ± 0.77</td>
<td>0.53 ± 0.03</td>
</tr>
<tr>
<td>Dark§ &amp; Dark§</td>
<td>0.41 ± 0.50</td>
<td>0.31 ± 0.35</td>
<td>0.48 ± 0.04</td>
</tr>
<tr>
<td>1572 &amp; 1325</td>
<td>0.40 ± 0.76</td>
<td>0.32 ± 0.77</td>
<td>0.53 ± 0.03</td>
</tr>
<tr>
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<td>0.48 ± 0.04</td>
</tr>
</tbody>
</table>

\* See Figure 8.
§ See Figure 11.
were normalized for section thickness to give the final spectra.

**Results**

The overall electron microscopic appearance of the pigment epithelium in the posterior retina of the pearl mutant differed greatly from that of wild-type. The number of melanosomes in pe/pe was greatly reduced, in confirmation of the previous light-microscopic observation. Some melanosomes also displayed very irregular boundaries with clumps of melanin at their peripheries. The basal RPE membrane did not exhibit infoldings over the entire extent of the cell. The basal lamina of the pigment epithelial cell (the innermost layer of Bruch’s membrane) also showed a periodic structure in some areas, in contrast with the overall amorphous appearance displayed in most wild-type laminae. Otherwise, these genotypes were similar in number of nuclei per cell (2), appearance and distribution of mitochondria, and presence of phagosomes. In both genotypes, junctional complexes...
Fig. 7. Electron micrographs from superior (A) and inferior (B, C) retinas of pearl mutant animals showing retinal pigmented epithelial cells (RPE) and rod outer segments (OS). Note the scarcity of apical melanosomes in both aspects of the RPE and the incompleteness of basal membrane (BM) infoldings in the inferior RPE. Melanosomes exhibiting irregular profiles with peripheral clumps of melanin (arrowheads, B, C) are another mutant characteristic. Transverse sections (A and B, x9,800; bar = 1 μm) (C, x26,200; bar = 0.5 μm).

were present at the apical borders of the cells. This article concentrates upon the differences in melanosomes and basal membrane.

Melanosomes

Previous studies in rodents\textsuperscript{7,14,15} demonstrated regional differences in the abundance of melanosomes. Therefore, we compared the pigment epithelial cells in superior and inferior retinas of wild-type animals for differences in the melanosome location, size, numerical density, and volume density. The uncorrected density of melanosomes seen in sections (Fig. 3) was 10–30% greater in the inferior retina. Also striking were the larger size (Fig. 4) and greater volume density (Table 1) of the melanosomes in the inferior retina. Moreover, the fraction of apical melanosomes was much less in the inferior retina (13%, Table 1) than in the superior retina (32%), and the apical melanosomes were located farther from the basal membrane of the superior retina than of the inferior retina (Fig. 5A). The distributions of location of soma melanosomes showed a greater number of melanosomes located closer to the basal membrane in the inferior retina than in the superior retina (Fig. 5B). Thus, marked melanosome differences exist between inferior and superior retinas of wild-type ani-
Fig. 8. Distribution of diameters of soma melanosomes of pearl mutant retinas compared with that of wild-type retinas (inferior retinas, light-adapted). Note the larger size for pearl mutant.

Electron microscopic examination of the pearl retina (Fig. 7) showed that very few melanosomes were present in the apical processes, and that the soma melanosomes were larger and less abundant than those of wild-type. The pearl melanosomes were also located closer to the basal membrane than those of wild-type. These observations were confirmed by quantitative analysis. The percentage of melanosomes in the superior apical processes was only 4.9% for pearl versus 31% for wild-type (Table 2). In the inferior retina of pearl a mere 0.7% of the melanosomes were located in the apical processes, compared to 13% in wild-type (Table 2). The soma melanosomes were as large as 1.1-μm diameter in the inferior retina of pearl, but were not larger than 0.9-μm diameter in wild-type (Fig. 8). The numerical density of soma melanosomes of pearl was only about one fifth of the melanosome density in the corresponding retinal location of wild-type (Table 2). The decrease of numerical density more than offset the larger size of the pearl melanosomes, for the volume density of melanosomes in the soma of pearl was less than one half that of wild-type for both superior and inferior retinas (Table 2). The soma melanosomes of pearl tended to lie closer to the basal half of the cell, whereas those of wild-type tended to lie closer to the apical half (Fig. 9). Thus, the location, size, and frequency of occurrence of melanosomes of the pigment epithelium of pearl mutants differed greatly from those of wild-type.

We searched for differences in the concentration of melanin within the melanosomes of pearl and wild-type by measuring the specific absorption of the central region of the largest, most fully melanized melanosomes that we were able to find in unstimulated, unstained sections. For individual wild-type melanosomes, the maximal specific absorption ranged from 0.9 to 1.3 nm−1 in a broad peak from 470 to 500 nm (Fig. 10). We detected no significant differences between the shapes of the absorption spectra or the absorption maxima from inferior versus superior retina or from pearl versus wild-type (Fig. 11). Thus, the absorption spectra of the largest, most fully melanized melanosomes of pearl mutants were indistinguishable from those of wild-type.

Basal Membrane

The basal membrane of the pigment epithelial cell is characterized by numerous infoldings that make its surface area considerably larger than the surface area of the apposing Bruch's membrane (see Zinn and Benjamin-Henkind,16 Fig. 1.8). We observed that for wild-type mice infoldings occurred over virtually the entire extent of the basal membrane that we studied (Fig. 2A). The average boundary length density (Bₐ, length of infolding boundary per area measured, see Materials and Methods) in a tangential plane through the regions of infoldings in the inferior retina was 12.3 (±0.2 SEM) μm⁻¹ for the wild-type retina. For the inferior retinas of pearl mutants the boundary length density (Bₐ) of the area with infoldings was only 10.1 (±0.7 SEM) μm⁻¹. These values cannot be used directly to compute the functionally important surface area of the infoldings per unit volume occupied by the basal membrane (surface density, Sᵥ, Weibel,11 p. 30) because the sectioned infoldings have various shapes in both transverse and tangential sections. However, irrespective of the shape of the sectioned
objects, surface density, $S_v$, is directly proportional to boundary length density, $B_A$. Due to this direct proportionality, the ratio of boundary length densities obtained for pearl and wild-type is equivalent to the ratio of the values of their surface densities ($pe/pe^+:+/+:1.1:12.3$), but only for regions which exhibit infoldings. In order to compare the surface densities of the entire posterior region of the inferior retina, two variables must be considered: infolding height and basal area covered by infoldings. The average height of the infoldings (measured in transverse sections) was not identical for the two groups. The
Fig. 11. Spectra of average specific absorption of melanosomes from inferior and superior retinas of pearl mutants and wild-type animals. Note the similarities between these spectra.

height was 0.95 (±0.03 SEM) \( \mu m \) for ++/+ and 1.1 (±0.16 SEM) \( \mu m \) for pe/pe. Furthermore, the pearl mutant did not exhibit basal infoldings over the entire extent of its RPE; only 80% of the basal surface area was comprised of infoldings (Fig. 2B). Therefore, the corrected ratio of surface densities can be expressed as \( \text{pe/pe} : \text{++/+} : 10.1 \times 0.8 \) (area correction): \( 12.3 \times 0.86 \) (height correction). Consequently, in the inferior part of the posterior retina, pearl exhibits a basal membrane area which is approximately 0.76 of the corresponding area of wild-type. Infolded lateral membranes were also noted between some of the pearl RPE cells but not between wild-type cells.

Desmosome-like attachment sites between basal infoldings, as previously described for the rat, \(^{17}\) were also observed in the mouse. These membrane specializations joining adjacent folds of the basal membrane appeared to be more numerous in the RPE of the wild-type mouse compared to the pearl mouse.

The basal laminae of the RPE of wild-type mice were composed of an amorphous substance (Fig. 12A). However, most of the pearl mice exhibited foci of periodic fibers in the basal laminae. Depositions of periodic fibers were especially prominent in regions where the basal infoldings covered deep impressions in the RPE (Fig. 12B). In these regions two fibrous components were evident: parallel sheafs of fine fibrils interconnected perpendicularly with dense bands at intervals of 0.08 to 0.12 \( \mu m \) (Figs. 12B, C). Cross-striated fibrous arrays were apparent in all of the basal laminae of pearl superior retinas that were examined, but this characteristic was only noted in 57% of their inferior retinas. In cases where the superior and inferior retinas of the same pearl eye were examined, basal laminae of the inferior RPE of three mice did not show periodic fibers, although the fibers were evident in the basal laminae of the corresponding superior RPE. Hence, of the 15 pearl retinas examined, 13 (87%) contained fibrous arrays in a thickened basal lamina. These fibers occurred in both light- and dark-adapted retinas.

**Discussion**

The regional differences in total (uncorrected) melanosome number detected in wild-type mice are comparable to differences found in the rat. \(^7,^{14}\) It is noteworthy that less pigmentation is present in the superior retina of the mouse, which a greater fraction of apical melanosomes is located (Table 1). The fewer soma melanosomes and the greater numbers of melanosomes in the apical processes could be due to the migration of more melanosomes to the apical processes in the superior retina. Because of the different melanosome distributions in the superior and inferior halves of the retina, it is essential to know what region is being examined when evaluating light/dark effects. Our findings on the location of the melanosomes, in light-adapted and dark-adapted animals at the same time of day, confirm the finding that light-induced migration of the melanosomes of the pigment epithelium does not occur in mammals. \(^{18}\)

A significant difference between ++/+ and pe/pe is the virtual absence of melanosomes in the apical processes of the RPE of pe/pe. This study also demonstrates that melanosomes in the apical processes of the murine RPE do not respond to light by moving more vitreal into the apical processes (the “shading phenomenon” found in certain poikilotherms, see Burnside and Laties, \(^{18}\)). However, we are unable to suggest any functional deficit due to the lack of melanosomes in the apical processes of the RPE of pe/pe.

According to a general scheme for melanosomal development, \(^{19-21}\) the early stages of melanosomal formation, ie, the synthesis of the protein backbone and of melanin itself, occur while the melanosome lies close to the basal membrane of the pigment epithelial cell; the melanosome is roughly spherical in form at this stage. Further maturation of the melanosome involves its transition to an ellipsoidal form and its movement toward the apical membrane and into the apical processes when they develop. If
Fig. 12. Electron micrographs of the basal regions of RPE cells of wild-type (A) and pearl mutant (B, C) retinas. The wild-type basal membrane is extensively folded and overlaid with a thin basal lamina (arrowheads). No fibrous components are evident in the extracellular spaces between infoldings (A). The pearl basal membrane lacks infoldings in a region adjacent to a deep invagination between RPE cells (B). A thin basal lamina (arrowheads) lies over the flattened basal membrane while a thicker basal lamina containing striated structures is evident in the space between cells and in an area surrounding basal infoldings (arrow). Higher magnification of another area shows a pearl RPE cell (outlined by its limiting membrane, arrowheads) in close apposition to extracellular material which is not membrane bound (C). The extracellular deposit is composed of an amorphous background which envelops sheafs of parallel fibers overlaid with dense striations of a regular periodicity of 0.08-0.12 μm. The enhanced contrast of C was obtained by staining with 7% uranyl acetate in methanol. Transverse sections (A and B, ×19,400; bar = 1 μm) (C, ×51,500; bar = 0.5 μm).
this scheme is accepted for wild-type animals, then our measurements of pearl melanosomes are consistent with development that is arrested at an early stage: the melanosomes become fully melanized, as evidenced by their nearly normal specific absorption; the shape of the melanosome profiles is spherical, rather than elliptical; and the melanosomes are located closer to the basal, not the apical, membrane. The basal accumulation of melanosomes of the pearl mutant is similar to that of the dilute mutant, but the visually induced eye movements of the dilute mutant are normal, while those of pearl are not. The highly irregular profiles containing clumps of melanin in many pearl melanosomes could be the result of melanin degradation, although extreme melanin degradation, as reported in the hypopigmented mutants, was not evident.

Fibrous components with a periodicity similar to that found in the mutant mouse have been observed in the basal lamina of the RPE from various sources: senescent human, immature human with Menkes' kinky hair disease; senescent rat; and in the extracellular basal matrix produced by cat RPE in vitro. In senescent humans the periodic striations were described as resembling "in vitro preparations of short-segment, long-spacing collagen." The cultured cat RPE cells were shown to synthesize labeled peptides characterized as \( \alpha_1 (IV) \) and \( \alpha_2 (IV) \) collagen. However, no direct evidence is available to show that the extracellular bundles of periodic fibers found in pearl mutants consist of collagen.

The basal infoldings of the RPE have been shown to be structurally modified in diseased and senescent states. In streptozotocin-diabetic rats, the infoldings exhibit an increase in basal membrane surface area. In senescent mice and humans the basal membrane surface area is reduced due to the decreased number of basal infoldings. All of these alterations of the basal membrane have been suggested to affect RPE function.

Two components of the retina, the basal lamina of Bruch's membrane and the basal RPE cell membrane, influence the transport of molecules to and from the retina. The anionic sites of the basal lamina act as a molecular filter capable of binding cationic molecules. The basal RPE cell membrane has been shown to transport several substances important for RPE function.

References

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