Vitreous

Bruch’s membrane

Retinal pigment epithelium
and the visual cycle

Retinal degenerations and pigment epithelium

Basic Science course 2017
Swiss Eye Week, Neuchâtel

Ch. E. Remé, Zürich
The Vitreous
The vitreous body is not a passive “filler” but fulfills important active physiological functions!
The vitreous is not only a passive filling substance but fulfills active physiological functions

Weight: 4 gr
Volume: 4 ml
Composition: 98% water
Glycosaminoglycans: Hyaluronic acid, heparan sulfate
Collagen fibrils
Cells

• Glycosaminoglycans account for structural properties of vitreous.

• The vitreous gel selectively regulates permeability, among other molecules also oxygen distribution within the eye!

• Vitreous liquefaction increases oxygen tension which may lead to oxydative stress.

• Cells in the vitreous are “guardians” against bacterial infections.
Anatomical Features
Cloquet’s canal

Cloquet’s canal is the only remnant of the primary vitreous and can transport cells and molecules.
Anatomical Features
Attachments of vitreous

Anterior vitreous membrane

Vitreous base

Peripapillary attachment

Macular attachment
Age-related changes of the vitreous with clinical significance

- **Syneresis**: fluid filled cavities and collapse of gel
- Collagen fibers condense (*mouches volantes, floaters*)
- Vitreous retraction (*shrinkage*)
- Posterior vitreous may **detach**
- Incomplete posterior vitreous detachment may cause **retinal tear, retinal detachment or vitreous hemorrhage**
- Vitreous liquefaction reduces regulation of molecular transport
Complete (A) and incomplete (B) vitreous detachment. OCT shows vitreous detachment and macular edema.
Bruch’s Membrane
Bruch’s membrane is built of various collagen components. Thickness: 2 - 4 μm

- PE basal infoldings
- PE basement membrane
- Inner collagenous layer
- Elastic layer
- Outer collagenous layer
- Choroid basement membrane
Aging of Bruch’s membrane:

**Stratified deposits:**

- **Basal linear deposits**, between PE basement membrane and inner collagenous layer of Bruch’s membrane.

- **Basal laminar deposits**, between PE and its basement membrane.

**Focal deposits, drusen below PE:**

- **Hard drusen**

- **Soft drusen**

Thickness of Bruch’s membrane doubles with age.
Aging changes in the outer retina are a significant risk factor for AMD

Sclerosis / loss of choroidal vessels
Thickening of choroid

Stratified deposits and drusen in Bruch’s membrane

Lipofuscin accumulation in PE

Lesions / loss of photoreceptors

Secondary lysosome accumulation in inner segments (autophagy)
Deposits and drusen can predispose for AMD

Basal laminar deposits and drusen.

Their lipids are a diffusion barrier into and out of the PE and retina for hydrophilic molecules and retinol (Vitamin A).

<table>
<thead>
<tr>
<th>INTO PE and retina</th>
<th>oxygen, molecules (retinol, glucose, lipids).</th>
</tr>
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<tbody>
<tr>
<td>OUT OF retina and PE</td>
<td>water, “waste” of retinal metabolism.</td>
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Drusen.

Their components may constitute an inflammatory stimulus and/or induce autoimmune complexes which sustain chronic inflammatory reactions in predisposed individuals.
Drusen in Bruch’s membrane

OCT

Electron Microscopy

PE

Bruch’s membrane

Drusen
Confluent drusen in AMD
The pigment epithelium
The pigment epithelium plays a major role in the pathogenesis of multifactorial age related macular degeneration!
Photoreceptors and pigment epithelium (PE) form a functional unit!

When photoreceptors die, PE cells will subsequently die. When PE cells die, photoreceptors will follow.

Gene mutations in one tissue can lead to the death of the other with ensuing retinal – PE degeneration.
Pigment epithelial cell

- Apical processes
- Rod outer segments
- Lysosome
- Phagosome
- Mitochondria
- Nucleus
- Basal infoldings
Pigment epithelial cell (PE)
The PE is one of the most active phagocytotic systems of our body

Photoreceptor side

Choroidal side

Mitochondria

Phagosomes (Heterophagy)

Autophagy
Autophagy (self-eating) segregates and degrades cytoplasmic organelles. It recycles molecules, protects against damaging molecules and may fuse with phagosomes.

AV is increasingly recognized as a universal and important cellular metabolic process.
Apical processes with melanin granules and Actin filaments for phagosome engulfment. 
Apical phagocytic surface with integrin\(\alpha_v\beta5\), CD36 and MERTK.

Apical plasma membrane with 
Na/K ATPase, transporter, cotransporter, exchanger, channels: ion movements.

Basolateral membranes with channels, cotransporter, exchanger: ion movements.

Tight junctions (zo) constitute blood-retinal barrier
Zonula adhaerens (za) for cell adhesion
Gap junctions (gj) for cell to cell communication
Desmosomes (d) for cell adhesion

Integrins for PE cell adhesion
CD36 for signalling.
Major functions of the PE

Absorption of stray light.

Protection against oxidative stress.

Transport:
- nutrients (retinol, glucose, lipids)
- ions
- oxygen
- water

Visual cycle, i.e. visual pigment regeneration.

Phagocytosis of discs and autophagy.

Secretion:
- growths factors (PEDF, VEGF)
- cytokines, chemokines
Failure of any of those functions leads to retinal / PE degeneration!

Strauss O., 2005
Failure of water transport out of retina leads to macula oedema. Altered pH influences water transport. Altered ion homeostasis influences electrical responses (EOG; ERG).

Strauss O, 2005
The polarity of PE cells is vital for their function and health! That means apical or basal or baso–lateral direction for:

- Transport.
- Secretion.
- Visual cycle.
- Phagocytosis.
- Exocytosis.
Pause !!
The functional range of the visual system of humans and some mammals is remarkably broad spanning over 11 logarithmic units.

### Illuminance levels (lux)

<table>
<thead>
<tr>
<th></th>
<th>Sun disc</th>
<th>Day light</th>
<th>Room light</th>
<th>dawn</th>
<th>Full moon</th>
<th>Star light</th>
</tr>
</thead>
<tbody>
<tr>
<td>100’000</td>
<td>10’000</td>
<td>400 - 1000</td>
<td>10 - 400</td>
<td>0.3 - 10</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

**Cone vision**
- **photopic**

**Rod/cone vision**
- **mesopic**

**Rod vision**
- **scotopic**
How rods and cones work in vision:

Cones: fast responses, responsive at high illuminance

BRIGHT LIGHT

- colour vision
- high resolution
- low sensitivity

Rods: slow responses, saturation

DIM LIGHT

- no colour vision
- low resolution
- high sensitivity