Guest author Univ.-Prof. Dr. med. Peter Heilig: RETINAL PIGMENT EPITHELIUM (RPE)
September 1, 2024 ub_admin 447 views
RETINAL PIGMENT EPITHELIUM (RPE)
Author: Univ.-Prof. Dr. med. Peter Heilig

"The most fascinating cell" *of the retina is "the retinal pigment epithelium"* according to experts (1). The RPE would not be 'outside' the retina. No – an integral part of the retinal system would be the RPE cell, especially as an inseparable functional unit with peripheral receptors – via microvilli – with a *"thick basal cushion of mitochondria"* and the interphotoreceptor matrix. It does not separate – on the contrary, it connects, via ion channels, via the transport (*'transport epithelium'*) of nutrients and metabolites and external segment phagocytosis.

The *'nonsynaptic interface'* between RPE and the outer receptor segments, complex and in optimal extent, is described as the first *microconnectome* of the visual system. Basolateral folds increase the area by a factor of about ten. Loss of these folds and accumulations of extracellular matrix etc. – at these points – are signs of retinal aging processes (2). The RPE ensures a perfect pumping function (*Na,K-ATPase*) and adapts to the retinal requirements as well as to those of the choriocapillaris.

Both RPE and photoreceptor cells are postmitotic and must therefore function flawlessly throughout life. The phagocytosis of the outer segment fragments in the morning light represents an extraordinary burden: "RPE cells are the most strongly phagocytic cell type in the body". The phagocytic surge triggered by an orchestrated 'signaling': *"Eat me"* must be stopped quickly and the receptor fragments must be completely 'digested'. *Undigested residues, 'autofluorescent lipofuscingranules',* would be toxic. Ion channels regulate circadian rhythms of phagocytosis.
Ion channels can be used to cause diseases (*channelopathies*) in RPE failure, for example in dystrophies and other hereditary and immune-associated problems. *„Cancer cells can stop their growth by 'Ca^{2+} driven growth factor secretion'".* Light causes a transient increase in extracellular retinal fluid volume – ATP energy operates Na and K as well as Cl during transepithelial transport$^{+\,+\,-}$ including fluid exchange. The highly sensitive cell-fluid-volume regulation takes place via volume-sensitive Cl channels.

Light reduces the subretinal K concentration and *releases "a previously unknown 'light surge' substance that binds to a receptor on the apical membrane of the RPE",* which leads to an increase in transepithelial Cl transport and higher transepithelial basolateral negative potentials, which can be registered electro-oculographically (EOG). A variety of various growth factors (e.g. VEGF-A) and cytokines are secreted by the RPE. Interactions with the photoreceptors and the endothelium of the choriocapillaris guarantee regulation and stability as well as the integrity of the photoreceptors including retinal neurons.$^{+}$
Toll-like receptors (TLR) immune recognition (or sentinel) molecules – recognize microbial molecular pathogen patterns. TLRs demonstrate the importance of RPE in terms of innate immunity, immune regulation, and adaptive ocular immunity. The RPE cell *"can act as a first responder in infection attacks"* and "respond with *adaptive response to a second antigen exposure"* (immunological memory).
Cytokines: pro-inflammatory, immunosuppressive; Stimulation with cytokines causes high VEGF production. RPEs can become a source of chemotactic cytokines – chemokines and adhesion molecules. Subsequently – recruitment of leukocytes and local profibrotic and proangiogenic processes as well as fibrovascular membranes and*traction* by myofibroplastic-differentiated Müller cells.

Pigment epithelium-derived factors (PEDF) inhibit proliferative tendencies under normal conditions. However, hyperglycemic and hypoxic factors can inhibit this PEDF expression.
Phototoxic stimuli can not only irreversibly damage receptors and RPE, but also fragment mitochondria: *"Mitochondrial dynamics were disrupted with characteristics of fusion-related obstruction after blue-light irradiation"* (3)
Myopia: RPE is significantly involved in the regulation of eye growth with synthesis and secretion of growth factors, receptor expression and activation of neurotransmitters, ion exchange and fluid movement, especially through its inductive *switch position* between retina and choroid.

RPE cells: a 'pluraletantum'; they function like a highly organized single – great cell.
VEGF: Vascular Endothelial Growth Factor, constitutively expressed by the RPE; most important angiogenic growth factor, maintenance of RPE, choriocapillaris, etc. Triggers hypoxia, oxidative stress, hyper- or hypoglycemia, hyperthermia.

Embryonic development: Loss of just a single VEGF allele can have fatal consequences.
Chronodisruption: light bursts at an inopportune time: put an undue strain on the system and can trigger undesirable long-term effects such as a false ski track on an avalanche slope.

Epilogue: The RPE needs to be treated with care. May it be spared from unphysiological (artificial) light tortures. One day, reason will prevail – pleasantly warm light will delight the eyes and never dazzle or distract – improve contrast vision and make *you forget about phototoxicity*.
"We will not live to see it" (Cassandra).

References
1 Klettner, K., Dithmar S. (Eds.) (2024) The Retinal Pigment Epithel – Physiology and Pathology. Knight
2 Lindell M et al (2023) Volumetric Reconstruction of a Human Retinal Pigment Epithelial Cell Reveals Specialized Membranes and Polarized Distribution of Organelles. Invest Ophthalmol Vis Sci; 64(15):35.
3 Zhang C et al (2024) High correlated colour temperature artificial lighting impairs retinal pigment epithelium integrity and chloride ion transport: A potential mechanism for choroidal thinning; Biochem Biophys Res Com 718,150078
Gender: beyond
Interest: no conflict

_____

Event: **Perceived** 15.10.24 at 19.00 h
at the Otto-Mauer-Zentrum - KAVÖ
, Währinger Str. 2-4, A-1090 Vienna

_____

Conflict of interest:
The author declares that there was no conflict of interest in the sense of the recommendation of the International Committee of Medical Journal Editors in the preparation of this article.
Correspondence address:
Univ.-Prof. Dr. med. Peter Heilig
Ophthalmology and Optometry
peter.heilig@univie.ac.at