



The **CREA**tion of the Department of Physical Chemistry of Biological Sys**TE**ms [CREATE]

666295 — CREATE — H2020-WIDESPREAD-2014-2015/H2020-WIDESPREAD-2014-2

Prof. Chris Dainty

Institute of Ophthalmology
UCL, UK

Adaptive Optics in Vision Science: A Look Back ... and Forwards

Adaptive optics, combined with other imaging modalities such as optical coherence tomography, is on the threshold of a dramatic breakthrough in retinal imaging: being able to image every single cell in the retina. In this talk I shall trace the history in the “modern” era, from 1997 onwards, when adaptive optics transitioned from being exclusively in the domain of big science and the military, to becoming a (relatively) low cost technology. In looking at the past, what can we say about the future of adaptive optics in vision science?

Prof. Karl-Wilhelm Koch

University of Oldenburg
Germany

Biophysical approaches to understand biomolecular interactions in vision

Signal transduction in visual cells is mediated by a network of protein-protein interactions triggered by conformational changes in signaling proteins. Biophysical techniques like surface plasmon resonance, fluorescence spectroscopy and backscattering interferometry are crucial tools to investigate the sensory signal flow in rod and cone cells.

Prof. Arie-Lev Gruzman

Bar-Ilan University
Israel

Fighting retinal degenerative diseases with RPE65-inhibitors

In order for the brain to acquire visual information, light couples in the retina to a sensitive protein called rhodopsin, which changes its conformation and transmits a signal to the visual cortex in the brain. Continuously sustaining this process requires that the rhodopsin returns to its active form. This is carried out a by complex chain of chemical and biological



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reactions. However, in some undesirable cases, toxic molecules are generated in excess (retinal dimer and A2E), which in turn lead to severe degenerative damage to the retina. These conditions (such as Age-Related Macular Degeneration and Stargardt disease) are considered to account for a large percentage of today's blindness globally. In this work, we propose to combat these degenerative diseases using a family of fluorinated chiral β -aminoalcohol molecules which would act as inhibitors for Retinal Pigment Epithelium enzyme (RPE65) and thus reduce the concentration of these toxic moieties. We synthesized 16 fluorinated molecules based on the scaffold of (R)-emixustat, which has already shown promising results as RPE65 inhibitor. The addition of a fluorine atom to (R)-emixustat in the ortho position resulted in a 4-fold increased potency of the compound.

Prof. Olaf Strauß

Charité University Medicine
Berlin, Germany

The retinal pigment epithelium: a partner in visual function and interface to the body system

The retinal pigment epithelium (RPE) is a close interaction partner of the photoreceptors in the retina. In this partnership the RPE maintains the photoreceptor's structural integrity, ion homeostasis in the retina and takes part in the visual function. At the same time it builds the outer blood/retina barrier that maintains the immune privilege of the retina and permits interaction with the body system. Failure of RPE's function or pathologic influence on the RPE lead to retinal degeneration. Mutational changes of bestrophin-1, a Ca^{2+} -dependent Cl channels exclusively expressed in the RPE lead to Best's vitelliform macular dystrophy, a hereditary form of central vision loss and with juvenile onset. Mutant forms of bestrophin-1 fail to traffic into the plasma membrane and prevent at the same time also the trafficking of voltage-dependent Ca^{2+} channels. Both mechanisms might explain



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the electrophysiological alterations in retinal function and the accumulation of metabolic end products such as lipofuscin in the patient's RPE. On the other hand systemic pathologic conditions such as hypertension does not only affect the RPE's epithelial integrity. Moreover, with angiotensin receptors on the blood side the RPE reacts to changes in the systemic renin-angiotensin system. As a result the RPE takes up angiotensin-2 from the blood stream and accumulates it in the retina. In consequence, increased retinal angiotensin-2 levels lead to a group of pathologic alterations that are associated with hypertensive retinopathy. In summary, the RPE locally supports and maintains the function and integrity of photoreceptors. Moreover, the RPE provides an interface of the retina with the body system to fulfill new and for their physiological impact not understood tasks for retinal function.



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