Abstract DGA 2012

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Lichtstimulation in Neuroprothesen.

## Optogenetic stimulation of the retina

J. Duebel

Institut de la Vision, Paris, Frankreich

The insertion of light sensitive microbial opsins into retinal neurons is a promising approach to restore vision in retinal degenerative diseases, such as Retinitis pigmentosa. This disease refers to a diverse group of hereditary diseases that lead to incurable blindness, affecting two million people worldwide. As a common pathology, rod photoreceptors die early, whereas light-insensitive, morphologically altered cone photoreceptors persist longer. It has been unknown if these cones are accessible for therapeutic intervention. We show that expression of archaebacterial halorhodopsin in light-insensitive cones can substitute for the native phototransduction cascade and restore light sensitivity in mouse models of retinitis pigmentosa. Resensitized photoreceptors activate all retinal cone pathways, drive sophisticated retinal circuit functions (including lateral inhibition and directional selectivity), activate cortical circuits, and mediate visually guided behaviors. Using human ex vivo retinas, we show that halorhodopsin can reactivate light-insensitive human photoreceptors. Finally, we identified blind patients with persisting, light-insensitive cones for potential halorhodopsin-based therapy.