Optogenetics for Restoring Vision: From Mouse Models to the Patient Perspective

Degenerative retinal diseases lead to the irreversible loss of photoreceptors, while inner retinal layers often remain preserved until late in the disease course. Optogenetic gene therapy aims to restore vision by rendering the surviving neurons of the inner retina directly light sensitive, hence enabling them to substitute the function of the lost photoreceptors in the sense of a biological vision prosthesis. There has been significant progress in the field over now more than 15 years. Yet, the visual function restored in early clinical studies has remained somewhat limited.

The aim of our work is to systematically understand the factors currently limiting the performance of optogenetic vision as well as better defining the therapeutic niche of patients affected by advanced retinal degeneration that may be filled by optogenetics.

In this talk, I will discuss how our recent preclinical work, based on mouse models of retinal blindness combined with in vivo and ex vivo electrophysiological approaches, has identified bipolar cell-targeted delivery of optogenetic actuators as an important determinant of high-fidelity optogenetic vision. These studies also inform the potential consequences of therapeutic intervention at disease stages where optogenetically generated vision may still interfere with residual native visual function. We will also reflect on the limitation of such studies in short-lived animal models, that are not able to model the long term trajectory of retinal degeneration in humans and how this makes a better understanding of the perspective of affected individuals on such prosthetic gene therapies in general and on their motivations for trial participation necessary.