



Sonja Kleinlogel

Title:

Engineering photoreceptors into optogenetic tools for the control and understanding of cellular processes in microbial, animal and plant systems

Abstract:

Bistable rhodopsins are naturally photosensitive G-protein coupled receptors (GPCRs) that can be toggled between stable ON and OFF states using light. They are responsible for photosensitivity and vision across animals (including humans), and a potential source of powerful optogenetic tools enabling bidirectional control of influential intracellular signalling cascades across all body systems using light.

We have engineered chimeras between bistable rhodopsins and ligand GPCRs to light-sensitize the endogenous signalling cascade of retinal interneurons, the bipolar cells for the restoration of vision. We show that these chimeric Opto-mGluR6 proteins cluster into the location of the native mGluR6 signalosome and successfully trigger the mGluR6 signalling cascade provoking a strong physiological response when expressed *in vivo*. By delivering Opto-mGluR6 chimeras to the retinas of blind mice using a custom gene therapy with synthetic adeno-associated viral vectors and synthetic bipolar cell specific promoters, we were able to restore pattern vision approaching wild type values in treated blind mice. Remarkably, the treatment effect was independent of the time point of treatment as well as the time point of functional testing, suggesting that the optogenetic treatment stabilizes the process of degeneration.

In summary, we show that Opto-GPCRs can be successfully engineered to pave the way to receptor-targeted designer optogenetics.

Biography:

Professor Sonja Kleinlogel is a trained bioengineer and neurophysiologist leading the research group “Translational Optogenetics” at the Institute of Physiology at the University of Bern. Sonja is passionate about bringing basic research to patients in need. She pioneered the fields of optogenetics and vision restoration by engineering light-sensitive designer proteins and retinal gene therapies. She is inventor and founder of the Arctos Medical AG.

Sonja Kleinlogel received her MSc degree at the University of Bern working on therapies for the restoration of hearing and completed her PhD studies at the Vision Touch and Hearing Research Centre of the University of Queensland (Australia) working on color and polarization vision of invertebrates (mantis shrimp). After a Postdoc at the Max-Planck Institute for Biophysics in Frankfurt (Germany) she was appointed at the University of Bern in 2012 and received tenure in 2018.

Sonja Kleinlogel is committee member of the European “next-generation optogenetics” program and Co-PI in the ERC Synergy program on light sensitive G-protein coupled receptors. Professor Kleinlogel has received several innovation prizes, such as the Theodor Kocher Prize, the Euretina Prize and the SwissOphth Award. She is married, mother of two children and lives with her family in the Bern area.