Eye, and particularly the retina, is a “window into the brain”. It reveals sufficient information about patient condition, and for humans, it is the main organ responsible for world perception. The retina is a very fragile and complex structure, located on the back of the eyes and is exposed to many environmental hazards leading to its defects or even retinal degeneration (RD). In modern society, an increasing number of people suffering from visual impairment are being observed. The predominant causes of visual impairments are irreversible changes in the retinal structure and mutations leading to photoreceptor (our light detectors) death in the retina. Two main diseases related to photoreceptor death are retinitis pigmentosa and age-related macular degeneration which are causing blindness/vision loss in ~200 million people globally. Without question, these conditions significantly reduce the quality of life and, therefore, drive a strong need for developing new, easy to use and effective techniques for not only slowing down the disease progression but also restoring vision. There have been a large number of attempts aiming to prevent complete loss of photoreceptors or restoring vision by either opsin delivery or retinal transplantation. The viral gene therapy based on delivering light-sensitive ion channels to surviving retinal cells seems the most direct way of curing blindness. However, a number of issues remain to be solved in order to create an effective therapy. **The general aim of this project is to develop a new approach to deliver light-sensitive ion channels in order to restore selective neuronal responses to low light stimuli in the visual system of a blind animal.** To do so we will use a modified Rabies virus (RV) tracing technique that allows not only for efficient gene expression but also cell-type-specific network tracing to precisely deliver proteins of interest to the desired retinal circuit. This approach is crucial to obtain adequate light sensitivity and restore selective visually evoked responses in the brain. It will also create a specific functional network that will mimic the natural processing of the retina.

The Rabies virus will be used for opsin delivery into the degenerated retina to restore visual responses in the blind animals. Visual responses will be tested in the primary visual cortex for not only sensitivity to flash of light but also for selectivity to certain stimulus parameters like contrast, spatial frequency, orientation/direction, and size. It is crucial to investigate whether viral/gene therapy can restore selective neuronal responses in the visual system. We take full advantage of the hierarchical connectivity of the retinal network to target different functional circuits and information processing channels by infecting different retinal layers through monosynaptic viral tracing.

This unique method will reveal the extent to which the visual system will respond to complex stimuli like moving spots, drifting gratings, pattern motion, and natural stimuli after viral treatment.