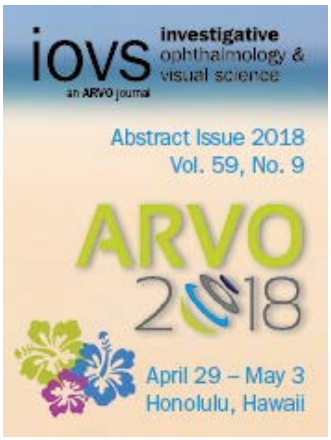

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Activity of iridium pyridine-based nanophotoswitches in retina

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Abstract

Purpose : Nanophotoswitches (NPSs) offer a new tool for optical stimulation of neuronal activity, in vitro and potentially in vivo. Our group previously reported a ruthenium bipyridine-based NPS (Rubpy-C17) that, after injection into the eyes of photoreceptor degenerated blind rats, elicited electrical activity in the contralateral superior colliculus upon light exposure. Compared with the ruthenium

complexes, the family of iridium complexes has been more widely used in clinics, owing to its biosafety profile. We have thus synthesized and tested Irbpy-C17, an analog of Rubpy-C17 with the ruthenium core replaced by iridium.

Methods : Rubpy molecules can be visualized by their luminescence upon visible wavelength illumination. To examine membrane incorporation, fluorescence imaging of HEK cells was obtained after incubation with Irbpy-C17. Activity of Irbpy-C17 was studied by MEA recording from wholemount retina after intravitreal injection. The test molecules were administered into the vitreous of blind RCS rats at the concentration of 200 µM. Animals were kept in dark after injection until the surgical dissection of retina. Acutely isolated retina was mounted on the MEA with the ganglion cell layer facing down to capture the spiking activity in response to light stimuli.

Results : Irbpy-C17 exhibited good membrane incorporation similar to that of Rubpy-C17. Interestingly, despite that Irbpy-C17 elicited minimal light response initially, subsequent application of synaptic blocker cocktail that pharmacologically isolated RGCs substantially enhanced the light activation of RGCs (1.8 ± 0.3 fold increase in spike frequency). In comparison with the 3-hour incubation between injection and dissection, prolonged 24-hour incubation led to a more pronounced 2.5 ± 0.5 fold increase in spike frequency.

Conclusions : Our data suggest that Irbpy-C17 may act on multiple components of the retinal neural circuitry that could suppress its direct action on RGCs via synaptic transmission. These molecules intravitreally administered remain stable and active in the ocular environment up to at least one day post injection. These data will prompt us to further study the iridium complexes in parallel with the ruthenium counterparts, particularly for the underlying mechanism of their differential behavior. The NPSs obviates the need for gene manipulation or toxic UV illumination, highlighting its potential in generating high-acuity prosthetic vision in the blind.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.