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Toxicity of Transition Metal Complex-based Nanophotoswitches in Retina

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Abstract

Purpose : Nanophotoswitches (NPSs) based on transition metal complexes offer a new tool for optical stimulation of neural activity in photoreceptor degenerated retina. We previously reported robust light-elicited neural activity in degenerate retinae exposed to ruthenium bipyridine based NPSs (Rubpy-C17) and its iridium analog (Irbpy-C17).

Irbpy-C17 was developed as an alternative to Rubpy-C17 for the biosafety properties of the iridium complexes. Here we present a study of the toxicity of both NPSs in rodent retinae.

Methods : Toxicity of Rubpy-C17 was tested in wildtype C57BL/6J mice and Irbpy-C17 in wildtype Long Evans rats. Animals were intravitreally injected with the test molecules (up to 50 μM) and sacrificed at different time points post injection: 3, 7, 14 and 28 days, respectively. Retinae were obtained, fixed and sliced for histological analysis immediately after animal euthanization. H&E staining was performed to examine morphological integrity of retina and TUNEL staining performed to detect apoptosis of retinal cells. For comparison, Ru(bpy)3]Cl2 injection and sham surgery were included for control.

Results : H&E staining revealed no detectable sign of morphological or structural changes in the retinae after prolonged exposure to either Rubpy-C17 or Irbpy-C17 versus the control. There was no significant reduction in the thickness of different nuclear and plexiform retinal layers or the density of retinal neurons ($p<0.05$), nor was there evidence of significant aggregation of immune cells. TUNEL staining showed minimal occurrence of cell apoptosis in the NPS treated retinae, similar to the control ($p<0.05$). No longitudinal changes in either the morphology or the cell apoptosis was observed with the post injection time.

Conclusions : Overall our data did not find ocular toxicity associated with either the ruthenium or the iridium based NPSs within the concentration range tested. The results obtained with both complexes are similar to that obtained with the control molecule [Ru(bpy)3]Cl2, which lacks a membrane-anchoring 17 carbon chain attached to the bipyridine group, indicating that the inclusion of the carbon chain did not enable NPSs entry into the cells, nor did it cause apoptotic response. The present study provides new evidence of biosafety of our NPSs in rodent retinae, further encouraging developing NPS-based molecular retinal prosthesis to potentially restore high-acuity prosthetic vision in the blind.

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