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DEVELOPING NOVEL OPTOGENETIC TOOLS FOR THE TREATMENT OF RETINAL DEGENERATIONS

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Purpose: Optogenetics holds a tremendous potential for curing blindness secondary to inherited retinal degenerations. Unfortunately, efficient, therapeutically relevant transduction of target cells, the bipolar cells, has not been achieved representing a major obstacle for developing this form of treatment. The goal of this proposal is to develop adeno-associated viral (AAV) vector based delivery system to target optogenetic molecules to bipolar cells with high specificity and expression strength for the purpose of treating blindness. Methods: AAV vector libraries were generated by standard molecular biology protocols. Vectors will be used to drive expression of human opsins to ON-bipolar cells via intravitreal and subretinal delivery to adult *C57* wild-type and degenerated *rd*^{1} eyes. 6 weeks post injection eyes will be harvested and embedded into agarose gel. Retinal cross-sections will be processed, immuno-stained and examined under confocal microscopy to confirm and quantify expression. Results:
Three different AAV viral capsids (AAV2/2-7m8, AAV2/2-4YF and AAV2/8-BP2) have been successfully produced and packaged with opsins in combination with ON-bipolar specific promoter. We are currently performing intraocular injections and the efficacy of ON-bipolar cell transduction will be determined in future work as described above. Conclusions: We have successfully generated AAV vector libraries to target optogenetic candidates to ON bipolar cells. Achieving high-levels of optogene expression in bipolar cells has potential to restore useful visual function, setting the stage for future trials in human patients. Financial Disclosure: *"Funding for this research was supported by the Global Ophthalmology Awards Program (GOAP), a Bayer-sponsored initiative committed to supporting ophthalmic research across the world"*