

[Print this Page](#)

Presentation Abstract

Program#/Poster#: 3898

Abstract Title: **Restoring Visual Function in Adult Rd1 Mice Using Virally-Delivered Channelrhodopsin**

Presentation Start/End Time: Wednesday, May 06, 2009, 9:45 AM -10:00 AM

Location: Grand Floridian A

Reviewing Code: 207 gene therapy and delivery - BI

Author Block: *A. Horsager*^{1,2}, *J. Liu*³, *E.S. Boyden*^{4,1}, *A.C. Arman*², *B.C. Matteo*¹, *A.P. Sampath*², *W.W. Hauswirth*³. ¹Eos Neuroscience, Inc., Los Angeles, CA; ²Zilkha Neurogenetic Institute, University of Southern California, Los Angeles, CA; ³Ophthalmology, University of Florida, Gainesville, FL; ⁴MIT Media Lab, Massachusetts Institute of technology, Boston, MA.

Keywords: 537 gene transfer/gene therapy, 685 retina

Abstract Body: **Purpose:** Channelrhodopsin (ChR2) is a light-sensitive protein that, when expressed in mammalian neurons, depolarizes the tissue in response to light activation. Using cell type-specific promoters, expression of ChR2 can be genetically-targeted so as to activate specific neural circuits. We show that behavioral and physiological visual function is restored in the adult rd1 mouse when ChR2 expression is genetically-targeted to the ON bipolar cells using the GRM6 promoter, and delivered using an adeno-associated virus (AAV).

Methods: We evaluated retinal bipolar cell transduction using wild-type and capsid-mutated AAV serotypes. Vector, including the ChR2 and green fluorescent protein (GFP) genes, was either subretinally or intravitreally injected in two month old rd1 mice under the control of the CBA or GRM6 promoter. GFP expression and localization was evaluated using confocal microscopy coupled with immunohistochemistry 2 weeks later. Next, visual function was measured in wild-type, rd1 untreated, and rd1 ChR2-treated mice using the Morris water maze, and through in vitro retinal patch clamp recordings.

Results: Two wild-type serotypes were effective at transducing retinal bipolar cells. However, capsid-mutated serotypes were able to increase bipolar cell transduction by as much as 20-fold, even with an intravitreal injection. In the water maze task, the ChR2-treated mice learned the task nearly as well as the wild-type mice (the rd1 untreated mice did not learn the task). Bipolar and ganglion cells recordings show that depolarization in these cells can be mediated by ChR2 activation.

Conclusions: Expression of ChR2 in ON bipolar cells, delivered using AAV in adult rd1 mice that have lost nearly all photoreceptors, restores behavioral and physiological function. Equally as important, it is possible to target ChR2

expression to bipolar cells using a capsid-mutated AAV, even with an intravitreal injection. Further research is necessary to evaluate perceptual threshold and visual acuity in these treated animals.

Commercial Relationships: **A. Horsager**, Eos Neuroscience, Inc., E; Patents, P; **J. Liu**, None; **E.S. Boyden**, Eos Neuroscience, Inc., E; Patents, P; **A.C. Arman**, None; **B.C. Matteo**, Eos Neuroscience, Inc., E; Patents, P; **A.P. Sampath**, None; **W.W. Hauswirth**, AGTC, Inc., E; Patents, P.

Support: EY11123, EY13729, EY07132, NS36302, FFB, MVRF, Eos Neuroscience, Inc.

©2009, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to www.iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at arvo@arvo.org.