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Bio-energetic preservation of cones in a mouse model of retinitis pigmentosa

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Abstract

Purpose : Recent studies suggest cone degeneration in retinitis pigmentosa (RP) may occur due to intracellular energy depletion. We test the hypothesis that cones die from energy depletion by examining the effect of bio-energetic agents on cone survival in the Rd1 mouse model of retinitis pigmentosa.

Methods : Two different bio-energetic therapies were tested: local glucose and systemic oral creatine. Mice (C3H/HeJ; Rd1) in the glucose study received daily unilateral subconjunctival injections of 50% glucose for 30 days (n=18); control mice received osmolarity-matched subconjunctival saline injections (n=18). Fellow eyes served as untreated controls. Mice in the creatine study were placed on a 2% creatine diet (n=18); control mice received a standard diet without creatine (n=18). Mice in both studies were sacrificed either at 45 or 60 days age. Cone density was quantified on whole-mount retinas using OPN1SW fluorescent labelling. Mean cone densities between treatment and control groups were compared using Student's t-tests.

Results : An initial experiment characterised the natural history of cone degeneration in C3H/HeJ mice (Fig 1). Cone density was significantly greater in 2% creatine mice compared to standard-diet mice at 60 days (1696 ± 218 vs. 1347 ± 150; mean ± SD; p = 0.01). Cone density was significantly greater in saline injected eyes compared to un-injected eyes at 60 days (1643 ± 77 vs. 1359 ± 205; p = 0.02). There was no significant difference in cone density between glucose injected and saline injected eyes at 60 days (1714 ± 202 vs. 1643 ± 77; p = 0.6).

Conclusions : These data suggest that cone degeneration in RP might occur due to energy depletion and that bio-energetic therapies may provide benefit. However,

glucose injections did not offer any benefit over saline injections. Further investigation will be needed to elucidate the mechanisms through which systemic creatine treatment and local saline treatment preserve cones.

This is an abstract that was submitted for the 2016 ARVO Annual Meeting, held in Seattle, Wash., May 1-5, 2016.

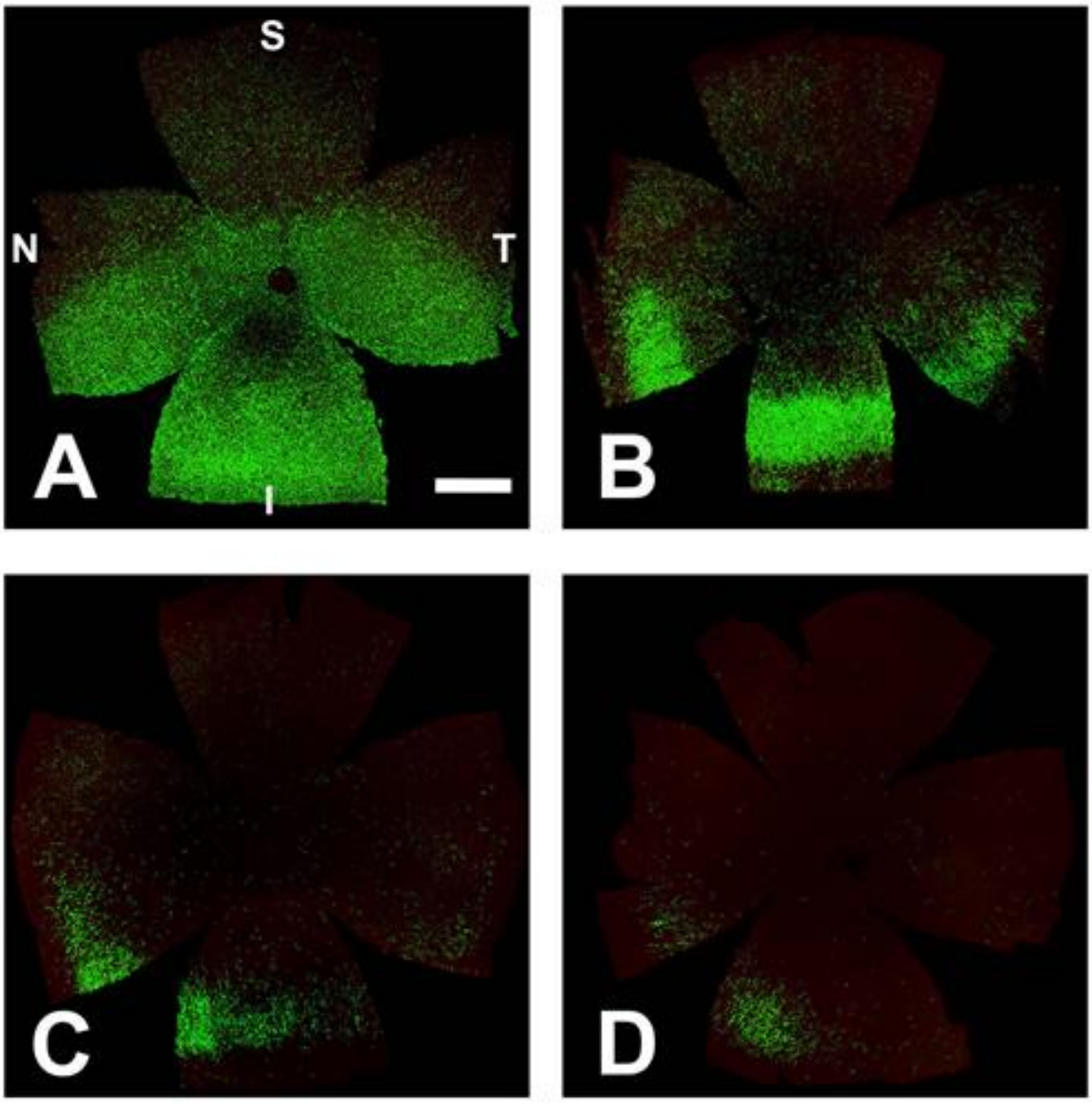

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Figure 1.
OPN1SW fluorescent immunollabelling in whole-mount Rd1 retinas over time. Images are taken at the ages of 14 days (A), 45 days (B), 150 days (C) and 300 days (D). The density of cones decreased over time from superior to inferior and temporal to nasal.

Approximately one-quarter of cones had degenerated by 45 days and half had degenerated by 60 days (data not shown). These times were chosen as end-points for the final study. Scale bar A = 1 mm.