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Functional Attenuation Coefficient Imaging of Rod Inner Segment: The Shape of Things to Come

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Purpose: Dysfunction of mitochondria and their linked processes within the rod cell (i.e., the rod energy-landscape) are leading hypotheses for rod atrophy in retinitis pigmentosa (RP). It remains unclear how to translate the detailed information available from isolated cell / mitochondria studies into how mitochondria are functioning and responding to treatment *in vivo.* Here we present a new rod energy-landscape biomarker that can help address this problem using a common clinical tool.

Methods: In mice, OCT data was converted into attenuation coefficients (AC) to map the light-scattering of mitochondria within the inner segment (IS), which fills ~75% of its volume and dynamically changes in response to energy needs. The IS AC shape profile is measured in an unbiased manner using an ellipse descriptor to generate a minor:major aspect ratio (AR).

Results: AC processing substantially improved within-animal, test-retest, and between-group reproducibility compared to the original OCT data. The IS AC AR was larger in the dark (i.e., relatively higher energy needs), and following phosphodiesterase 6 inhibition, than in the light (i.e., relatively lower energy demands) or following saline, respectively. Further, in *Pde6b*^{rd10} mice, a model of RP, the IS AC shape profile is abnormally low, and is corrected with neuroprotective treatment.

Conclusion: Our first-in-kind data raises the possibility of using the IS AC AR as a new treatment response biomarker of the photoreceptor energy-landscape using a clinically-available tool.