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ARVO Annual Meeting Abstract | July 2018

Expression and distribution of mitochondria, glycolytic enzymes, lactate dehydrogenase isoenzymes and lactate transporters in the vascular retina.

Robert Casson; John Peter Wood; Glyn Chidlow

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science July 2018, Vol.59, 2650. doi:

Abstract

Purpose : The “bioenergetic profile” of individual cell types within the retina remains incompletely understood. We aimed to investigate the expression and distribution of mitochondria, glycolytic isoenzymes and lactate transporters in the individual cell types of the rodent and marmoset retina.

Methods : Using a combination of immunohistochemistry, qPCR and western blotting, we examined the distribution and expression of mitochondrial proteins, glycolytic isoenzymes, and lactate transporters in the retinas of Murinae (rats and mice). Parallel analyses were performed on Callithrix Jacchus (common marmoset). We also examined lactate dehydrogenase activity in the rat retina via enzyme histochemistry and isoenzyme separation.

Results : In the rodent, retinal ganglion cells, amacrine cells and horizontal cells displayed similar metabolic profiles with unequivocal expression of hexokinase I, adolase A, GAPDH, c-enolase, PKM1 and the LDHB subunit. Bipolar cells were associated with intense expression of hexokinase I, adolase, GAPDH, c-enolase, PKM2, and the LDHA subunit. Photoreceptors displayed similar traits to bipolar cells. Müller cells expressed weak or undetectable labeling for all glycolytic isoenzymes. The RPE stained weakly for glycolytic enzymes, but expressed LDHB. LDH activity was intense in photoreceptor inner segments, both plexiform layers, and the RPE, while the isoenzyme distribution in the retina showed a decreasing gradient from LDH5 to LDH1.

The lactate transporter MCT1 localised to photoreceptor inner segments, the RPE and Müller cell processes. MCT4, was restricted to bipolar cells. The retinas of mice lacking photoreceptors (rd1 strain) expressed a dramatically lower level of hexokinase II mRNA, but a higher level of LDHB mRNA, relative to wild-type mice. All eight mitochondrial proteins analyzed displayed identical distributions in the rodent: enriched in both plexiform layers, photoreceptor inner segments and the RPE. Overall, the marmoset retina and RPE resembled the rodent retina in terms of metabolic profile.

Conclusions : The current findings advance our understanding of the unique metabolism of the vascularised rodent and primate retina and will assist in developing "bioenergetic" strategies to manipulate retinal metabolsim and treat retinal diseases.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.