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Expression and distribution of mitochondria, glycolytic isoenzymes and lactate transporters in the avascular retina: implications for retinal metabolism

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Abstract

Purpose : To shed light on the energetic demands and metabolic adaptations of the individual cell types of the rabbit and guinea pig retina.

Methods : Using a combination of immunohistochemistry, qPCR, and Western blotting, we determined the distribution and expression of mitochondrial proteins, glycolytic isoenzymes, and lactate transporters in the retina of the rabbit and guinea pig. In addition, we examined lactate dehydrogenase activity in the rabbit retina via enzyme histochemistry and isoenzyme separation.

Results : Overall, rabbit and guinea pig displayed remarkably similar metabolic profiles. Mitochondrial proteins (complex IV, cytochrome C, SOD2, Hsp60, pyruvate dehydrogenase, peroxiredoxin-3, mitochondrial pyruvate carrier 1) were highly enriched in the photoreceptor inner segments and the retinal pigment epithelium (RPE). Somewhat surprisingly, all of these proteins were also detectable within the inner retina, most notably in retinal ganglion cells.
Analogous to the vascularized rodent retina, certain glycolytic isoenzymes, such as hexokinase I, aldolase A, γ-enolase and PKM1, localized to both inner and outer retinal neurons in the avascular retina. Unlike the vascularized rodent retina, however, Müller cells in the rabbit and guinea pig displayed robust expression of various glycolytic isoenzymes including GAPDH, aldolase C and PKM2, as well as both LDH subunits. The RPE stained weakly for glycolytic enzymes, but expressed LDHB. The lactate transporter

MCT1 was widely distributed within the avascular retina and RPE, whilst MCT4 (the isoform associated with lactate efflux from glycolytic cells) was restricted to the inner retinal layers. Compared to rat retina, expression of LDHB, MCT1 and MCT4 mRNAs were higher in rabbit retina (when normalised to a pool of housekeeping genes), whilst LDHA was similar, and hexokinase II was considerably lower. LDH activity was particularly intense within photoreceptor inner segments and the nerve fiber layer, while the isoenzyme distribution in the rabbit retina revealed a greater amount of LDH1 when compared to the vascularized rat retina.

Conclusions : The current findings advance our understanding of the metabolic similarities and differences between vascular and avascular retinas.

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