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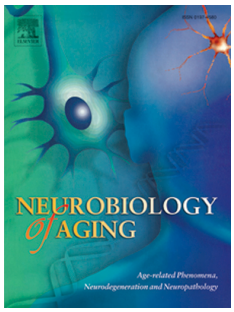

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Metabolic signature of the aging eye in mice

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Running title: Metabolic changes in the aged eye

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ABSTRACT

Aging is a major risk factor for age-related ocular diseases including age-related macular degeneration (AMD) in the retina and retinal pigment epithelium (RPE), cataracts in the lens, glaucoma in the optic nerve, and dry eye syndrome in the cornea. We used targeted-metabolomics to analyze metabolites from young (6 weeks) and old (73 weeks) eyes in C57 BL6/J mice. Old mice had diminished electroretinogram responses and decreased number of photoreceptors in their retinas. Among the 297 detected metabolites, 45-114 metabolites are significantly altered in aged eye tissues, mostly in the neuronal tissues (retina and optic nerve) and less in cornea, RPE/choroid and lens. We noted that changes of metabolites in mitochondrial metabolism and glucose metabolism are common features in the aged retina, RPE/choroid and optic nerve. The aging retina, cornea and optic nerve also share similar changes in NAD, 1-methylnicotinamides, 3-methylhistidine and other methylated metabolites. Metabolites in taurine metabolism are strikingly influenced by aging in the cornea and lens. In conclusion, the aging eye has both common and tissue-specific metabolic signatures. These changes may be attributed to dysregulated mitochondrial metabolism, re-programed glucose metabolism and impaired methylation in the aging eye. Our findings provide biochemical insights into the mechanisms of age-related ocular changes.

1. Introduction

As we age, the eye undergoes a gradual decline of visual function. This age-related visual deterioration is a combination of structural changes in the ocular tissues including the cornea, lens, retina, retinal pigment epithelium (RPE), choroid and optic nerve. With aging, the number of corneal endothelial cells declines and the epithelium-derived glands including the lacrimal and meibomian glands decrease their production of tears to lubricate the cornea (Gambato et al., 2015; Gipson, 2013; Mustonen et al., 1998). The aging lens decreases its ability to change shape (presbyopia), which is most likely attributed to modifications in the cortical fibre cells (Duncan et al., 1997; Salvi et al., 2006). The populations of neurons in the retina decrease with loss of visual acuity and sensitivity (Lei et al., 2011; Nadal-Nicolas et al., 2018). The microcirculation in the macula, the cone photoreceptor-enriched central region of the retina also declines with age (Salvi et al., 2006). RPE loses melanin and lipofuscin deposits accumulate in the RPE (Delori et al., 2001; Sarna et al., 2003). Aged Bruch's membrane, the innermost layer of the