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Mfsd2a is a Transporter for the Essential Omega-3 Fatty Acid DHA in Eye and Important for Photoreceptor Cell Development

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Aims: Eye photoreceptor membrane discs in outer rod segments (OS) are highly enriched in rhodopsin and the omega-3 fatty acid docosahexaenoic acid (DHA). The eye acquires DHA from blood, but transporters for DHA uptake across the blood-retinal barrier (BRB) or retinal pigment epithelium (RPE) have not been identified. Mfsd2a is a newly described sodium-dependent lysophosphatidylcholine (LPC) symporter expressed at the blood-brain barrier (BBB) that transports LPCs containing DHA and other long-chain fatty acids. LPC transport via Mfsd2a has been shown to be necessary for human brain growth. We would like to determine if Mfsd2a is required for DHA uptake in eye.

Methodology: Immunofluorescence, Western blotting, fluorescein angiography, electron microscopy, microarray

Result: Mfsd2a is highly expressed in RPE in embryonic eye, before the development of photoreceptors, and to be the primary site of Mfsd2a expression in the eye. Eyes from Mfsd2a KO mice, but not endothelial-specific Mfsd2a deficient mice, were DHA deficient and had significantly reduced LPC-DHA transport *in vivo*. Fluorescein angiography indicated normal BRB function. Moreover, BBB was not leaky in Mfsd2a KO mice. Histological and electron microscopic analysis indicated that Mfsd2a KO mice exhibited a specific reduction in outer rod segment length, disorganised OS discs, and mislocalisation of and reduction in rhodopsin early in postnatal development without loss of photoreceptors. Although minor photoreceptor cell loss occurred in adult Mfsd2a KO mice, electoretinography indicated visual function was normal. Moreover, developing eyes of Mfsd2a KO mice had activated microglia and upregulation of lipogenic and cholesterogenic genes, which are likely adaptations to loss of LPC transport.

Conclusion: These findings identify LPC transport via Mfsd2a as an important pathway for DHA uptake in eye and for development of photoreceptor membrane discs. The location of Mfsd2a at the RPE raises the possibility that Mfsd2a transport function could be exploited for delivering small molecules to the RPE and retina.