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LOSS OF IMPG2 PARALOGS LEADS TO RETINAL DEGENERATION IN ZEBRAFISH DOUBLE KNOCK-OUT MODEL

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Retinitis pigmentosa (RP) is a major inherited retinal dystrophy characterized by progressive photoreceptor degeneration and visual impairment. Among the genetic causes, mutations in the interphotoreceptor matrix proteoglycan 2 (IMPG2) gene have been linked to autosomal recessive forms of the disease. IMPG2 is a key component of the interphotoreceptor matrix (IPM), a specialized extracellular environment essential for photoreceptor maintenance, structural support, and function. Disruption of this matrix is increasingly recognized as a critical driver of retinal degeneration.

Building on our previous work, in which we characterized zebrafish (Danio rerio) single-knockout models for impg2 paralogues (impg2a and impg2b) at 7 days post-fertilization (7 dpf) and 9 months post-fertilization (9 mpf), we extend our investigation to a more severe genetic condition. In this study, we analyzed impg2 double-knockout (DKO) zebrafish at the same developmental stages, using light microscopy and transmission electron microscopy to assess retinal morphology and ultrastructure. Preliminary observations, focusing on the central retinal region, suggest an early impairment of photoreceptor outer segment development. At 7 dpf, outer segments appear severely reduced or absent, while at later stages (9 mpf) they display a markedly disorganized and shortened morphology, indicative of compromised structural integrity. These alterations are consistent with a critical role of impg2 paralogues in maintaining IPM organization and proper photoreceptor architecture. Overall, this study strengthens the relevance of the zebrafish DKO model for investigating IMPG2-related retinal diseases and provides a valuable platform for future therapeutic strategies targeting extracellular matrix preservation.

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