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Inositol phosphatase in primary cilia and eye development

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Inositol 5-phosphatase INPP5E plays an important role in cilia development in the retina. Mutations of INPP5E cause Joubert Syndrome, which is characterized by retinal degeneration, renal cysts, polydactyly, and mental retardation. Previous studies have implicated primary cilia abnormalities in Joubert Syndrome, the function of INPP5E in cilia formation and retina development are still not known. Using antisense morpholino oligonucleotides, knockdown of INPP5E was performed in zebrafish and rescue experiments were done using wild type and mutant human mRNA. Immunofluorescence was performed to determine the ciliary localization in zebrafish embryos. We show that in zebrafish INPP5E morphants, embryos showed a dose-dependent phenotype of retinal degeneration, microphthalmia, and body axis asymmetry. The Inpp5e morphant zebrafish exhibited shortened and decreased cilia formation in the Kupffer's vesicle and pronephric ducts as compared to controls. Epinephrine-stimulated melanosome trafficking was delayed in the Inpp5e zebrafish morphants. The phenotypes were rescued by co-injection of wide type but not mutant human INPP5E mRNA. Our data support an important role of INPP5E in ciliary development and maintenance and provide a novel animal model to examine the function of retinal development.

Biography

Yang Sun has completed his MD, Ph.D. from Washington University in St. Louis and residency in Ophthalmology from Stanford University School of Medicine. He is the Assistant Professor of Ophthalmology at Indiana University, Indianapolis.

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