

Conservation as well as divergence in Mcidas function underlies the differentiation of multiciliated cells in vertebrates

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Abstract

Multiciliated cells (MCCs) differentiate hundreds of motile cilia that beat to drive fluid movement over various kinds of epithelia. In *Xenopus*, mice and human, the coiled-coil containing protein Mcidas (Mci) has been shown to be a key transcriptional regulator of MCC differentiation. We have examined Mci function in the zebrafish, another model organism that is widely used to study ciliary biology. We show that zebrafish *mci* is expressed specifically in the developing MCCs of the kidney tubules, but surprisingly, not in those of the nasal placodes. Mci proteins lack a DNA binding domain and associate with the cell-cycle transcription factors E2f4/5 for regulating MCC-specific gene expression. We found that while the zebrafish Mci protein can complex with the E2f family members, its sequence as well as the requirement and sufficiency for MCC differentiation has diverged significantly from Mci homologues of the tetrapods. We also provide evidence that compared to Gmnc, another related coiled-coil protein that has recently been shown to regulate MCC development upstream of Mci, the Mci protein originated later within the vertebrate lineage. Based on these data, we argue that in contrast to Gmnc, which has a vital role in the genetic circuitry that drives MCC formation, the requirement of Mci, at least in the zebrafish, is not obligatory.

Cover



Cover Legend:

Multiciliated cells (MCCs) bear from tens to hundreds of motile cilia on their apical surface, and these cilia beat rhythmically to drive fluid movement over epithelia. MCCs within the kidney tubule of the zebrafish embryo (top left), on the epidermis of *Xenopus* tadpole (top right) and within the mammalian airway (bottom) are illustrated. See article by Zhou et al. on the evolving role of the *Mcidas* protein in the development of MCCs in the vertebrates. Color pencil-on-paper artwork by Sudipto Roy.