

## Differential Evolution of Duplicated Medakafish *mitf* Genes

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### Abstract :

Gene duplication is a major force of evolution. One whole genome duplication (WGD) event in the fish ancestor generated genome-wide duplicates in all modern species. Coloration and patterning on the animal body surface exhibit enormous diversity, representing a mysterious and ideal system for understanding gene evolution. Surface colors and patterns are determined primarily by pigment cells in the skin and eye. Thus, microphthalmia-associated transcription factor (Mitf) as a master regulator of melanocyte development is excellent for studying the evolution of WGD-derived gene duplicates. Here we report the evolution of *mitf* duplicate, *mitf1* and *mitf2*, in the fish medaka (*Oryzias latipes*), which encode medaka co-homologs Mitf1 and Mitf2 of the mouse Mitf. Compared to *mitf1*, *mitf2* exhibits an accelerated sequence divergence and loses melanocytic expression in embryos at critical developmental stages. Compared to a *Xiphophorus* counterpart, the medaka Mitf2 displayed a reduced activity in activating melanogenic gene expression by reporter assays and RT-PCR analyses. We show that the medaka Mitf2 has the ability to induce melanocyte differentiation in medaka embryonic stem cells but at a remarkably reduced efficiency compared to the *Xiphophorus* counterpart. Our data suggest differential evolution of the medaka *mitf* duplicate, with *mitf1* adopting conservation and *mitf2* employing degeneration, which is different from the duplication-degeneration-complementation proposed as the mechanism to preserve many gene duplicates in zebrafish. Our finding reveals species-specific variations for *mitf* duplicate evolution, in agreement with enormous diversity of body coloration and patterning.

### Key Word :

*mitf*, gene duplicate, melanocyte, neural crest, pigmentation.