Shigeharu Kinoshita, J Aquac Res Development 2017, 8:8 (Suppl)
DOI: 10.4172/2155-9546-C1-016

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Molecular basis on the indeterminate growth observed in fish skeletal muscle

Mammalian skeletal muscles undergo a marked senescence called sarcopenia, the loss of muscle mass due to an age-related decrease in the number and size of muscle fibers. Sarcopenia is a serious incidence in human associated with an increasing aged population. In this regard, teleosts are attractive models because these have an indeterminate muscle growth, i.e., an successive production of neonatal muscle fibers until death. The natural occurrence of negligible senescence in teleost skeletal muscle presents potentially a powerful system through which a way to prevent from sarcopenia would be discovered. However, the molecular mechanisms responsible for the indeterminate muscle growth in teleosts are almost unknown. Here, we focused on the torafugu (*Takifugu rubripes*) myosin heavy chain gene, $MYH_{M2528\text{-}1}$, which is specifically expressed in neonatal muscle fibers accompanied with indeterminate muscle growth. We examined the flanking region of $MYH_{M2528\text{-}1}$ through an in vivo reporter assay using zebrafish (*Danio rerio*) and identified a 2100bp 5'-flanking sequence that contained a sufficient promoter activity to induce specific gene expression. Spatio-temporal expression of reporter gene by the promoter well overlapped with known myogenic zones functioning in teleost indeterminate muscle growth. A deletion mutant analysis revealed that the-2100~-600bp 5'-flanking sequence of $MYH_{M2528\text{-}1}$ is essential for the promoter activity. This region contained putative binding sites for several representative myogenesis-related transcription factors and nuclear factor of activated T-cell (NFAT), a transcription activator involved in regeneration of mammalian adult skeletal muscle. A significant reduction in the promoter activity was observed in the deletion constructs which lessened the number of the above-mentioned binding sites, suggesting the involvement of muscle regeneration system in indeterminate muscle growth. In this session, I will also discuss our recenct fidings about transcriptome of aged fish and accerelated aging observed in growth hormone trangenic fish.

Biography

Shigeharu Kinoshita started his Research Experience on the Stress Response of the Phytoplankton when he was a college student. Later on, he was involved in the analysis of zebrafish mutants showing defects in development of the nervous system as a Post-doctoral Fellow. Currently he is conducting Research at lab of Aquatic Molecular Biology and Biotechnology, The University of Tokyo. His research interest is in the life span and aging of vertebrates.

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