胎生期マウス舌発生過程における Nfix を介した筋分化制御

川本沙也華

Nuclear factor 1 X-type-associated regulation of myogenesis in developing mouse tongue

Sayaka KAWAMOTO

日本歯科大学大学院生命歯学研究科歯科基礎系専攻
（指導：添野雄一 教授）

研究指導：田谷雄二 准教授
（日本歯科大学生命歯学部病理学講座）

The Nippon Dental University, Graduate School of Life Dentistry at Tokyo
(Supervisor: Prof. Yuuichi SOENO)

Directed by
Associate Prof. Yuji TAYA
The Nippon Dental University, Graduate School of Life Dentistry at Tokyo,
Department of Pathology

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Abstract

Objectives: The tongue contains skeletal myofibers that differ from those in the trunk, limbs, and other orofacial muscles. However, the molecular basis of myogenic differentiation in the tongue muscles remains unclear. In this study, we conducted comprehensive gene expression profiling of the developing murine tongue.

Methods: Tongue primordia were dissected from mouse embryos at embryonic day (E)10.5–E18.5, while myogenic markers were detected via microarray analysis and quantitative polymerase chain reaction (PCR). In addition to common myogenic regulatory factors such as *Myf5*, *MyoD*, *myogenin*, and *Mrf4*, we focused on *Nfix*, which acts as a unique molecular switch triggering the shift from embryonic to fetal myoblast lineage during limb myogenesis. *Nfix* inhibition was performed using a specific antisense oligonucleotide in the organ culture of tongue primordia.

Results: Microarray and ingenuity pathway analyses confirmed the significant upregulation of myogenic signaling molecules, including *Nfix*, associated with the differentiation of myoblasts from myogenic progenitor cells during E10.5–E11.5. Quantitative PCR confirmed that *Nfix* expression started at E10.5 and peaked at E14.5. Fetal myoblast-specific genes, such as *Mck* and *Myh8*, were upregulated after E14.5, whereas embryonic myoblast-specific genes, such as *Myh3* and *Myh7*, were downregulated. When *Nfix* was inhibited in the organ culture of tongue primordia, subtle morphological differences were noted in the tongue. Such an observation was only noted in the cultures of E10.5-derived tongue primordia.

Conclusions: These results reveal the contribution of *Nfix* to tongue myogenesis. *Nfix* expression during early tongue development may play a vital role in tongue muscle development.