

Notchシグナルによる骨格筋可塑性と筋再生の制御

Roles of Notch signaling in regulating muscle plasticity and regeneration

○藤巻 慎¹、松本 智博¹、小野 悠介¹

○Shin Fujimaki¹, Tomohiro Matsumoto¹, Yusuke Ono¹

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1. Dept Muscle Dev Regeneration, Kumamoto Univ

Notch signaling is highly conserved signaling pathway regulating cell proliferation and differentiation in a variety of tissues. We have previously reported that Notch1 and Notch2 coordinately maintain the muscle stem-cell pool in the quiescent state by preventing activation and regulate stem-cell-fate decision in the activated state, governing adult muscle regeneration (Fujimaki et al., *Stem Cells*, 2018). We also found out that Notch2, but not Notch1, Notch3, and Notch4, is expressed in differentiated muscle fibers. Here we investigated the role of Notch2 in adult muscle fibers using muscle-specific knockout mice for Notch2 (N2-mKO) and transgenic mice that expressed a muscle-specific active form of Notch2 (N2ICD-mTG). N2-mKO mice grew normally and did not display significant phenotypes in normal condition. However, Notch2 deficiency in muscle fibers suppressed muscle atrophy induced by mechanical unloading and diabetes. We then stimulated muscle hypertrophy by synergist ablation. While both N2-mKO and wildtype mice displayed increases in muscle mass and cross-sectional area of plantaris muscle, the hypertrophic efficiency is higher in N2-mKO than wildtype mice. In contrast, N2ICD-mTG mice displayed significant muscle atrophy and muscle weakness. These results demonstrated that Notch2 expressed in muscle fibers plays a critical role in regulating muscle plasticity.