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Myostatin facilitates slow and inhibits fast myosin heavy chain expression during myogenic differentiation

Shihuan Kuang

Purdue University, USA

Abstract

Skeletal muscles in the limb and body trunk are composed of heterogeneous myofibers expressing different isoforms of myosin heavy chain (Myh), including type I (slow, Myh7), IIA (intermediate, Myh2), IIX (fast, Myh1) and IIB (very fast, Myh4). The abundance of fast and slow myofibers within a muscle affects the taste and quality of the meat product. However, it is unclear how specific combinations of myofiber types are formed and regulated at the cellular and molecular level. We report here that myostatin (Mstn) positively regulates slow but negatively regulates fast Myh isoforms. Mstn was expressed at higher levels in the fast muscle myoblasts and myofibers than in the slow muscle counterparts. Interestingly, Mstn knockout led to a shift of Myh towards faster isoforms, suggesting an inhibitory role of Mstn in fast Myh expression. Consistently, when induced to differentiate, Mstn null myoblasts formed myotubes preferentially expressing fast Myh. Conversely, treatment of myoblasts with a recombinant Mstn protein upregulated Myh7 but downregulated Myh4 gene expression in newly formed myotubes. Importantly, both Mstn antibody and soluble activin type 2B receptor inhibited slow Myh7 and promoted fast Myh4 expression, indicating that myostatin acts through canonical activin receptor to regulate the expression of Myh genes. These results demonstrate a role of myostatin in the specification of myofiber types during myogenic differentiation.

Biography

Shihuan Kuang received his Ph. D. from University of Alberta and trained as postdoctoral fellow at Washington University School of Medicine. He has published more than 50 papers in reputed journals.