Transposon control in satellite cells during quiescence and differentiation

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Abstract

Satellite cells are unipotent precursors to skeletal muscle cells and are responsible for the ability of the muscle to regenerate. These dormant cells play a vital role in the maintenance and the regeneration of the skeletal muscles and are an important target of therapies. Our RNA-seq data shows that transposable element (TE) activity changes significantly between the states of quiescence and early activation of the satellite cells. These changes are accompanied by a marked downregulation of the Krüppel-associated box zinc finger protein (KRAB-ZFP) gene clusters, a family of transcriptional repressors that have evolved in vertebrates to repress evolving TEs. Many of these ZFPs share a main corepressor, KAP1, which brings about genetic silencing of the TEs via histone methylation. We have identified several targets of ZFPs that may play a role in the quiescent state of the satellite cells. We are particularly interested in understanding the KAP1-ZFP-TE interaction in the satellite cells, the resulting biological changes that take place and how this influences the quiescent/activation states. We show that KAP1 knock-down in isolated myofibers increases the expression of Pax7, a quiescent marker of the satellite cells. We conclude that the activity of KAP1 and specific ZFPs may have important roles in the quiescent state of the satellite cells as well as their capacity to differentiate.

Keywords: KZFP, transposable element, satellite cell, skeletal muscle

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