

Scientists reveal relationship between Dek and Intron retention during muscle stem cells quiescence

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Researchers from Hong Kong University of Science and Technology revealed quiescent muscle stem cells possess intron retention (white) in their transcriptomes Credit: HKUST

Muscle stem cells, the reserve stem cell in the skeletal muscles, are responsible for muscle repair after damage. They are the 'regenerative



medicine' to cure muscle diseases and muscle damage. In a healthy uninjured condition, muscle stem cells are in quiescence, a dormant state, to preserve them. Whenever there is muscle damage, they will wake up instantly and contribute themselves to building new muscles.

If this dormant state is loosely controlled, <u>muscle stem cells</u> will be wasted when there is no need for repair. If this <u>dormant state</u> is kept too tight, the <u>muscle stem cells</u> will not wake up when they are needed to contribute to muscle repair.

How muscle stem cells control this balance of quiescence remains a topic of heightened interest. Recently, a team of scientists at the Hong Kong University of Science and Technology revealed that intron detention (IR) is a key to the mechanism—when stem cells enter quiescence exit, Dek releases conserved introns, which allow the cell to be activated.

"Using <u>skeletal muscle</u> stem cells, also called satellite cells (SCs), we demonstrated prevalent intron retention (IR) in the transcriptome of quiescent SCs (QSCs)," said Prof. Tom Cheung, lead researcher of the team and SH Ho Associate Professor of Life Science at HKUST. "Intronretained transcripts found in QSCs are essential for fundamental functions including RNA splicing, protein translation, cell-cycle entry, and lineage specification. Our analysis reveals that phosphorylated Dek protein modulates IR during SC quiescence exit."

While Dek protein is not present in QSCs, Dek overexpression in vivo results in a global decrease of IR, quiescence dysregulation, premature differentiation of QSCs, and undermined muscle regeneration. The researchers also found in their IR analysis on hundreds of public RNAseq data that IR is conserved among quiescent adult stem cells, which suggests that IR functions as a conserved post-transcriptional regulation mechanism that plays an important role during stem cell quiescence exit.



Their findings were published online in the journal *Developmental Cell* on June 4, 2020.

"IR has emerged as an important post-transcriptional regulatory mechanism supporting the complexity of gene expression regulation and cell-state transition," noted Prof. Cheung. "We observed around 1,200 genes possessing IR in QSCs, but in many transcripts, only selective introns were retained. The prevalence of IR among quiescent adult stem cells implies its functional importance in stem cell quiescence. Findings in the study will play a fundamental role in the field as scientists continue the quest to map out the mechanism of stem cell quiescence and stem cell-mediated tissue regeneration."

More information: Lu Yue et al, Dek Modulates Global Intron Retention during Muscle Stem Cells Quiescence Exit, *Developmental Cell* (2020). DOI: 10.1016/j.devcel.2020.05.006

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