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Mechanisms regulating muscle stem cells activation

Frédéric　RELAIX 教授

Paris Est-Creteil University, FRANCE

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研究所３号館１階　セミナールーム

ABSTRACT

Tissue resident stem cells are maintained quiescent in specialized niches and are capable to repair an organ following injury. Skeletal muscle stem cells, known as muscle satellite cells, are the indispensable cell population responsible of skeletal muscle homeostasis and regeneration in response to injury. In resting condition, the muscle satellite cells are quiescent, and upon niche disruption they rapidly exit quiescence towards an activated proliferative state. However, despite the identification of several molecular regulators of muscle stem cell quiescence and activation, the actual gene regulatory network regulating the initial transition between these cell states remains largely unknown. We implemented a fixation-based protocol to capture cells in their native state, and generated a high-resolution transcriptional map of muscle satellite cells early activation. By time-course analysis, we have captured the earliest transcriptional responses of in vivo quiescent stem cells, and uncovered kinetically co-regulated genetic modules that define a precise sequence of cellular processes that drive cells out of quiescence. Moreover, we found that in response to muscle injury, individual muscle stem cells react asynchronously yet follow a unique activation trajectory. Overall, our study proposes a mechanism of quiescence exit that obeys a precise series of biological function, whereby early proliferation signals act independently of the myogenic signals that occur later. Our findings will be discussed in the context of neuromuscular disorders and regulation of muscle stem cell function during tissue repair.

REFERENCES

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Relaix 教授は著明な骨格筋発生学、幹細胞生物学の研究者です。大阪大の中森博士の講演後、引き続き開催いたします。ぜひご聴講ください。担当・連絡先： 理事　武田　伸一（内線 5010）