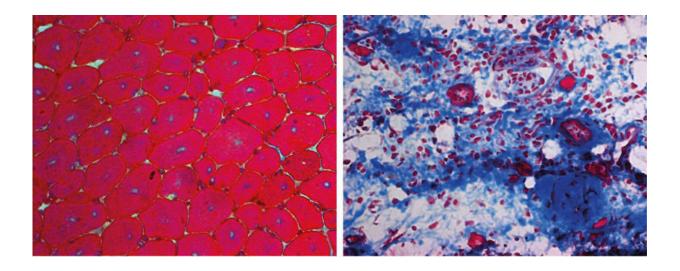


Gene controls stem cells during muscle regeneration

June 2 2015



Without Prmt5, the muscle does not heal: Cross-sections of tibial muscle tissue of mice after the tissue had been damaged by a cytotoxin. In the absence of Prmt5 (right), the process of muscle regeneration practically comes to a standstill and massive fibrosis becomes evident. In the control animal (left) individual regenerated muscle fibres are visible. Credit: MPI f. Heart and Lung Research

Unlike many other organs, skeletal muscles have a high potential for regeneration. When a muscle is injured, the muscle stem cells – also known as satellite cells – located between the individual muscle fibres rapidly begin to proliferate and subsequently replace the damaged muscles cells. Researchers from the Max Planck Institute for Heart and Lung Research in Bad Nauheim have recently discovered that a protein



called Prmt5 plays a key role in regulating the activity of these stem cells. Further studies are now being conducted to examine the impact of Prmt5 in muscle disorders.

The presence of satellite cells in skeletal muscles has been common scientific knowledge for decades. The small, spherical <u>stem cells</u> are located in the muscle, between the individual muscles fibres. In their normal state, they remain almost completely inactive. When a muscle is injured, however, they abruptly spring into action. Within a very short space of time, the satellite cells begin to proliferate, subsequently healing the injury by replacing damaged muscles fibres.

When satellite cells react to an injury, their transition from an inactive state to one of increased activity needs to be perfectly balanced. Uncontrolled proliferation of satellite cells in healthy <u>muscle tissue</u> increases the tumour risk. Conversely, <u>muscle regeneration</u> is impeded if the satellite cells are not activated quickly enough in case of an injury.

A team of scientists headed by Thomas Braun from the Max Planck Institute for Heart and Lung Research in Bad Nauheim has now identified a gene that plays a decisive role in regulating the activity of satellite cells. In isolated <u>muscle stem cells</u> taken from <u>mice</u>, the researchers identified 120 genes that are instrumental for the function of these cells.

The next step was to switch off one of these genes, Prmt5, in the satellite cells of adult mice. "In healthy mice, switching off Prmt5 in the satellite cells had no effect on the muscles. But when the mice had a muscle injury, the results were completely different", says Ting Zhang, the study's lead author. While the researchers did not observe any signs of regeneration in the latter case, the muscles of control mice with an active Prmt5 gene healed normally. "Instead of growing new muscle tissue, the mice without Prmt5 eventually developed clear signs of fibrosis".



The Max Planck researchers conducted further studies to examine how Prmt5 regulates muscle regeneration. In mice without Prmt5, the number of satellite cells was noticeably reduced. It appears the gene is an important factor in regulating the proliferation activity. Furthermore, the results indicated that Prmt5 also prevents <u>satellite cells</u> from dying prematurely and plays a key role in transforming them into functional muscle fibres.

The researchers in Bad Nauheim hope their study will also help them gain a better understanding of muscle disorders in humans. "The loss of muscle tissue in the absence of Prmt5 shows clear parallels to degenerative muscle disorders such as Duchenne muscular dystrophy", says Johnny Kim, a member of Braun's working group. The team now hopes that in future, mice lacking the Prmt5 gene can serve as models for this particular disorder. "But we also want to study the etiological effects of Prmt5 regarding the genesis of muscular hypertrophies and certain tumour types," Kim adds.

More information: "Prmt5 is a regulator of muscle stem cell expansion in adult mice" *Nature Communications*. DOI: 10.1038/ncomms8140

Provided by Max Planck Society

Citation: Gene controls stem cells during muscle regeneration (2015, June 2) retrieved 4 May 2024 from https://medicalxpress.com/news/2015-06-gene-stem-cells-muscle-regeneration.html

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