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Different cellular mechanisms behind regenerated body parts

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Scientists at Karolinska Institutet in Sweden have discovered that two separate species of salamander differ in the way their muscles grow back in lost body parts. Their findings on the species-specific solutions, published in the scientific periodical *Cell Stem Cell*, demonstrate there is more than one mechanism of tissue regeneration.

To carry out their study, the scientists labelled different cell types in two species of salamander in order to ascertain what kinds of cell give rise to new muscle tissue in salamanders that had lost a front leg. Salamanders are known for their remarkable ability to regenerate not only lost tails and other extremities but also the tissue of internal organs, such as the heart and brain. The traditional view is that the new tissue is formed from a population of stem cells activated when body parts are damaged; what they found, however, was that even though the two species were relatively closely related, this was true only for one.

"We show that in one of the salamander species, muscle tissue is regenerated from specialised muscle cells that dedifferentiate and forget what type of cell they've been," says principal investigator Dr András Simon at the Department of Cell and Molecular Biology. "This is an interesting cellular mechanism that destabilises cell specialisation and produces new stem cells, as opposed to the other species, in which the new muscles are created from existing stem cells."

In the dedifferentiating species, the capacity to regenerate tissue does not decline with age, which the scientists believe can be linked to their

ability to make new stem cells from muscle cells on demand. Human muscle is also regenerative, and damaged fibres are repaired effectively. However, in patients with muscular dystrophy (a group of disorders in which the muscles are gradually broken down), for instance, the body eventually cannot keep up with the loss of muscle tissue. A possible reason for this is that the number of functional muscle stem cells in these patients decreases over time, leaving the population too small to repair the damage. The findings from the salamanders are not yet applicable to humans, but the knowledge gained will one day help scientists understand how damaged or lost tissue is regenerated.

"It's important to study the process by which the salamander's muscle cells forget their cellular identity and how it's modulated," says Dr Simon. "It's also important to examine why their ability to regenerate is independent of age and the number of times the same tissue and body part has been regenerated."

More information: 'Fundamental differences in dedifferentiation and stem cell recruitment during skeletal muscle regeneration in two salamander species', Tatiana Sandoval-Guzmán, Heng Wang, Shahryar Khattak, Maritta Schuez, Kathleen Roensch, Eugeniu Nacu, Akira Tazaki, Alberto Joven, Elly M. Tanaka, András Simon, *Cell Stem Cell*, online 21 November 2013.

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