

# Restoring Balance: Tail regeneration in *Eublepharis macularius* and its implications for spinal cord treatment

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## Introduction

The presence of a tail represents a vital part in living beings. Their tails serve a purpose and are used in a variety of ways, specifically adapted to each animal's behavior and living environment. For cats, the tail acts as a counter balancing tool during their jumps. In primates and chameleons, tails are used for climbing trees and obstacles. Kangaroos incorporate their tails into their motion by using them as an extra "leg," while fish and other marine animals use their tails to propel themselves through water. However, the tail extremity is not only used for balancing and motion purposes: Many animals use their tail to scare away others and defend themselves. In contrast, in some animals, the tails (usually painted in colors throughout the spectrum and decorated with ornaments) are used to attract potential mates (Lenin, 2017). For the leopard gecko (*Eublepharis macularius*), its tail serves two significant purposes, one of them life giving and the other life-saving. Unlike other animals, the tail of the leopard gecko consists of a spinal cord (University of Guelph, 2017). The ability of re-growing the tail and therefore being able to regrow a part of the spinal cord, has inspired researchers to study the structure and this remarkable ability in *E. macularius*. Their findings and understanding of the gecko's remarkable ability to regenerate their tail not only contributes to better understanding of the animal itself but it has treatment implications for spinal cord injuries, especially in humans.

## The leopard gecko (*Eublepharis macularius*)

Leopard geckos are natural occurring in the eastern hemisphere through Afghanistan, Iraq, Iran, Northwest India as well as Pakistan. Their habitats consist of semi-dry to dry desert areas and grasslands. The gecko's body is yellow with irregular black spots, hence the name. Unlike other geckos, *E. macularius* features a segmented tail, movable eyelids surrounding vertical slit pupils, and clawed toes. Leopard geckos are nocturnal animals that shelter under rocks during daylight. Regarding their diet, leopard geckos are known to be very adaptable. In wild life, they consume small insects. Figure 1 features some photographic impressions of the leopard gecko. (Woods)



**Figure 1:** The leopard gecko (McLeod, 2017)

## The importance of the tail and managing predator escape

The leopard gecko's tail has two functions that are crucial for the survival of the animal: It acts as a storing feature for fat and when detached in the presence of a predator, will act as a distraction, allowing the gecko to escape the dangerous scene. The nerve endings in the separated tail causes it to twitch for a short time. Besides these two main purposes, the tail of *E. Macularius* features a remarkable characteristic: its ability to re-grow after a detachment. It is this feature that particularly sparked the interest of researchers at the University of Guelph and inspired them to study the cells behind the gecko's ability to regenerate its tail.

## Tail loss implications

The caudal autotomy, that is, the ability to self-detach the tail and regrow it, is a widespread feature in a majority of lizards. While the detaching process provides a chance of survival for the organism, it comes at a cost. The animal trades its resource stock for an increased chance of survival. It is known that the tail can weigh up to one quarter of the body's weight. Therefore, losing it results in the shifting of the center of mass in the gecko's body (Lenin, 2017). Since a tail loss has implications on the locomotion and the balance for the geckos, they compensate it by hunkering down to the ground, stiffening their pelvic girdles and flexing their extremities (Lenin, 2017). Being now closer to the ground, the geckos are forced to take shorter steps which results in decreased moving speed. As their tails regrow, the geckos regain their ability to move faster.

## The tail regeneration process

Researchers Lynn et al., 2013 have investigated under what conditions leopard geckos' tail regrows. Their results are surprising: For leopard geckos, the tail regeneration process represents a priority, even when resources are limited, since it foremost affects survival and reproductive success in the long term (Lynn, 2013). The tail re-growth process takes about 30 days and is the fastest known re-growth process among lizards.

Payne et al., 2017 studied what happens on the cellular and molecular level during the tail regeneration. More specifically, they investigated the neovascularization during the tail regrowth process. The researchers found that the tail regeneration incorporates the building of a blastema, which is an accumulation of proliferating cells at the location where the autotomy occurred (Payne, 2017). These cells will form the majority of the tissue in the regenerated tail. Furthermore, the research group showed that the blastema in *E. Macularius* is not avascular, that means, it is not characterized by the lack of blood vessels. Compared to the original tail, the blood vessel distribution differs in the regenerated tail. However, it again exhibits a hierarchical network of vessels with a variety of luminal diameters and tissue thickness. Using technology immunostaining, the researchers were able to determine the dynamic interplay between the involved growth factor and the protein in the outgrowth of the blastema and the differentiation of tissue. The involved proteins are the pro-angiogenic protein vascular endothelial growth factor and the anti-angiogenic protein thrombospondin-1 (TSP-1). Initially, the expression for VEGF is occurring while TSP-1 is inhibited. As the differentiation proceeds, the expression of VEGF decreases and the occurrence of TSP-1 becomes more abundant. (Payne, 2017)

Professor Vickaryous, a researcher at the University of Guelph, and his team are the first researchers to have uncovered the type of stem cells that are enabling the geckos to regrow their tails. Professor Vickaryous stated that he and his team knew that the tail in *E. Macularius* features a spinal cord, but it was unknown to them which specific cells were responsible for the rebuilding of such a structure. Professor Vickaryous and his team found that the tail not only contains a large number of stem cells but also a large number of proteins which support the growth of stem cells. The researchers simulated the presence of a predator by pinching the gecko's tail which caused the gecko to drop its tail. By studying the cellular level of the tail attachment location, the team found that the spinal cord features a special type of involved stem cells: the radial glia. Professor Vickaryous stated that these cells are normally "quiet." However, in the event of a tail detachment, the cells begin to express different proteins in order to initiate the building process of a new spinal cord. Once the new spinal cord is completely built, the stem cells go back to their "resting" state. (Vickaryous, 2017)

## Implication for spinal cord treatment in humans and further understanding of stem cells

The spinal cord represents a collection of nerves that are connected to the brain. The spinal cord is covered by the spinal canal which is surrounded by protective bones, the vertebrae. There are 31 pairs of nerve strands that connect the spinal cord with various body parts, including the extremities, the abdomen, and the chest. The nerve strands are channeling the signals coming from and going to the brain. This allows the brain to be connected to the entire body, controlling muscles and organs and receiving sensory information such as touch, temperature, pressure, and pain. Despite its protective layers, the spinal cord is very

sensitive to injury. Given its significance to the proper functioning of a living being, an injury can have fatal consequences for it. Spinal injuries are divided into two categories: complete and incomplete. A complete injury means a full loss of sensation and muscle function from the place of injury downwards, and an incomplete injury means that certain functions remain in the body parts below the location of the injury. Surprisingly, in contrast to other body parts such as our skin, the spinal cord does not inherent a function to repair itself when being damaged. Spinal cord injuries can arise from trauma, loss of the blood supply to it or through compression resulting from an accident, a tumor or an infection.

Compared to the *E. Macularius*' response, Professor Vickaryous explains, the response of a spinal cord injury in humans is quite different. In humans, the response to an injured spinal cord is the building of scar tissue and not new tissue formation. Although the scar tissue helps to seal the wound, this response prevents the regeneration of the spinal cord in the long term, which represents a major problem. (Vickaryous, 2017)

Professor Vickaryous and his team think that this response, coupled with the lack of the required cells for a regeneration process is the reason for the limited repair after a spinal cord injury. According to Professor Vickaryous, this particular study represents one part in a series of research on *E. Macularius* to investigate its regenerative ability of the central nervous system. According to Professor Vickaryous, the next study will investigate the gecko's ability to regenerate brain cells. (Vickaryous, 2017)

In conclusion, leopard geckos have the remarkable ability to regenerate tissue of their central nervous system. This represents the ideal case to study wound healing and development processes.

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