Origin of the long body of snakes discovered

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A snake embryo. Credit: Francisca Leal, University of Florida

For many years, researchers have been trying to understand the origin of the exceptionally long trunks that characterize the body of snakes. This is a mystery in terms of animal development that can shed light on the mechanisms controlling the tissues that form the trunk, including the skeleton and the spinal cord. A research team led by Moisés Mallo from Instituto Gulbenkian de Ciência (IGC, Portugal) now discovered the key factor that regulates trunk development in vertebrates and explains why snakes have such a strikingly different body. These findings, published in the latest edition of *Developmental Cell* and highlighted in its cover, may open new avenues to the study of spinal cord regeneration.

Despite obvious differences in size and shapes observed among different vertebrate animals, they all have bodies with a head and neck, a trunk and a tail. It is the relative size of each of these body sections what makes a large part of the body differences among these animals. Still, all vertebrates develop by consecutive phases, forming each region of the body in a specific order, from head to tail. The development is guided by genetic instructions that inform the beginning and the end of each body region's formation. Moisés Mallo's laboratory has been trying to crack the genetic code that controls trunk and tail development in vertebrates. In order to achieve it, they studied mice that had particularly long or especially short trunks. "We thought that the analysis of these animals could give us the key to unveil the code of trunk formation", says Moisés Mallo.

Their experiments led to the surprising finding that the key controller of trunk development was the Oct4 gene, one of the essential regulators of stem cells. Since many other vertebrates also have Oct4, this gene could

play similar roles in other animals and might even be responsible for the exceptionally long trunks of snakes. Rita Aires, first author of this study, explains: "We had found that Oct4 is the switch that leads to trunk formation, still we couldn't explain the different trunk length observed in vertebrates, particularly in snakes. Therefore, we tested if this switch was being turned on or off during different periods of embryonic development in snakes compared to mice."

The researchers discovered that the Oct4 gene was indeed kept active during a longer period of time in snakes when compared to other animals. They also showed that this resulted from changes in the snake genome that happened during reptile evolution, which placed the Oct4 gene next to a DNA region that keeps this gene in an "ON" state during long periods of embryonic development.

"The formation of different body regions works as a strong-arm contest of genes. Genes involved in trunk formation need to start ceasing activity so that the genes involved in tail formation can start working. In the case of snakes, we observed that the Oct4 gene is kept active during a longer period of embryonic development, which explains why snakes have such a long trunk and a very short tail", says Rita Aires.

Moisés Mallo further explains: "We identified a key factor that allows essentially unlimited growth of trunk structures, as long as it remains active. Now we will investigate if we can use the Oct4 gene and the DNA region that maintains its activity to expand the cells that make the spinal cord, trying to regenerate it in case of injury."

More information: Rita Aires et al, Oct4 Is a Key Regulator of Vertebrate Trunk Length Diversity, *Developmental Cell* (2016). DOI: 10.1016/j.devcel.2016.06.021

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