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A Genetic Perspective into the Progressive Loss of Limbs in Snakes

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A Genetic Perspective into the Progressive Loss of Limbs in Snakes

David Miller, Southern Maine Community College

Abstract

Snakes evolved into the limbless animals we know today due to gradual mutations that caused certain regulatory regions of their DNA to lose functionality. Axel Visel led a group of several scientists to determine which regulatory regions were responsible for this loss by using CRISPR to introduce the suspected snake Sonic hedgehog (Shh) limb enhancer region into mice *in vivo*. The Sonic Hedgehog region is highly conservative and rarely shows any mutations. The affected mice were born with truncated limbs which suggests that the snake version of the Sonic hedgehog limb enhancer region isn't functioning properly. Martin Cohn and Francisca Leal studied the Sonic hedgehog region in snakes separately and found that several mutations were present at transcription factor binding sites, which severely inhibited the transcription of this region. Determining the function of genes and the influence mutations have on them is crucial to understanding the growth and development of all life.



Figure 1: Snake Fossil with developed limbs (Reference 2)

Introduction

Snakes lost their limbs over many generations, suggesting a gradual increase of mutations in one or more region of DNA. CRISPR can be used to observe the function and expression of similar regions of DNA as phenotypic traits in developing life across different species.

Method

- The sequence of the ZRS limb enhancer and Sonic hedgehog regions were read and compared among several different animals
- Experimentation was done to determine the relationship between the ZRS limb enhancer and Sonic hedgehog regions
- CRISPR-editing was performed on mice to determine the functionality of the snake version of the ZRS limb enhancer region

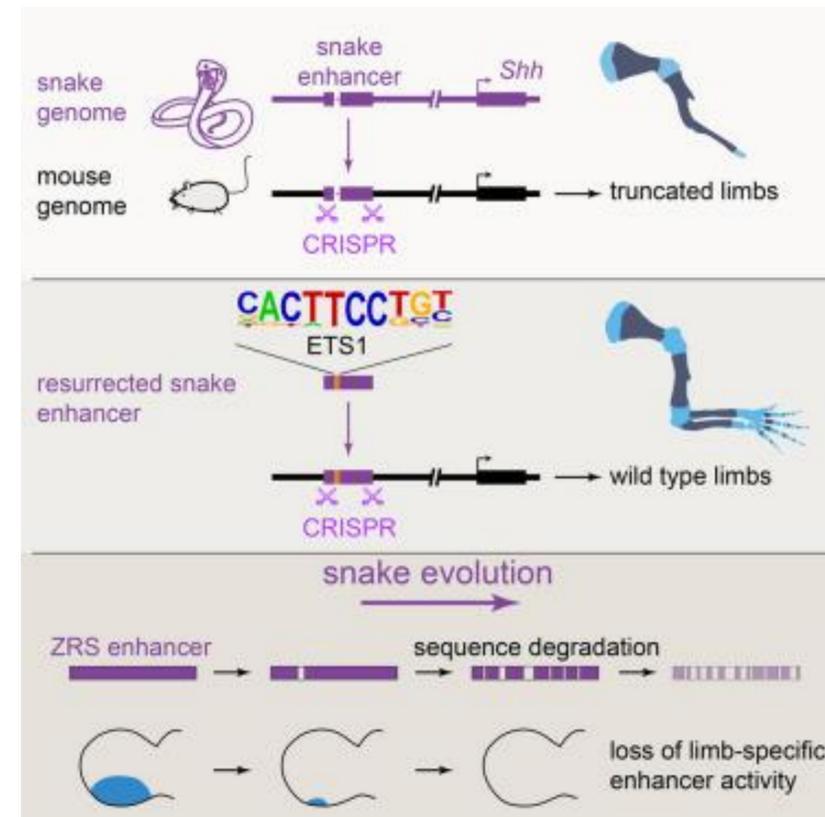


Figure 2: CRISPR-edited genes and the resultant limbs (Reference 3)

Results

- While the Sonic hedgehog gene is highly conserved, the ZRS region is more susceptible to mutations
- Snakes lost their limbs over time due to the progressive mutation of the ZRS region, reducing the transcription of the Sonic hedgehog gene
- When the snake variant of the ZRS region was introduced into embryonic mice, the limbs were underdeveloped
- When a fully functioning ZRS region was introduced to embryonic snakes, limb development was observed.

Conclusion

- The functionality of the ZRS limb enhancer determines the level of Sonic hedgehog gene transcription
- The level of Sonic hedgehog gene transcription influences embryonic limb development

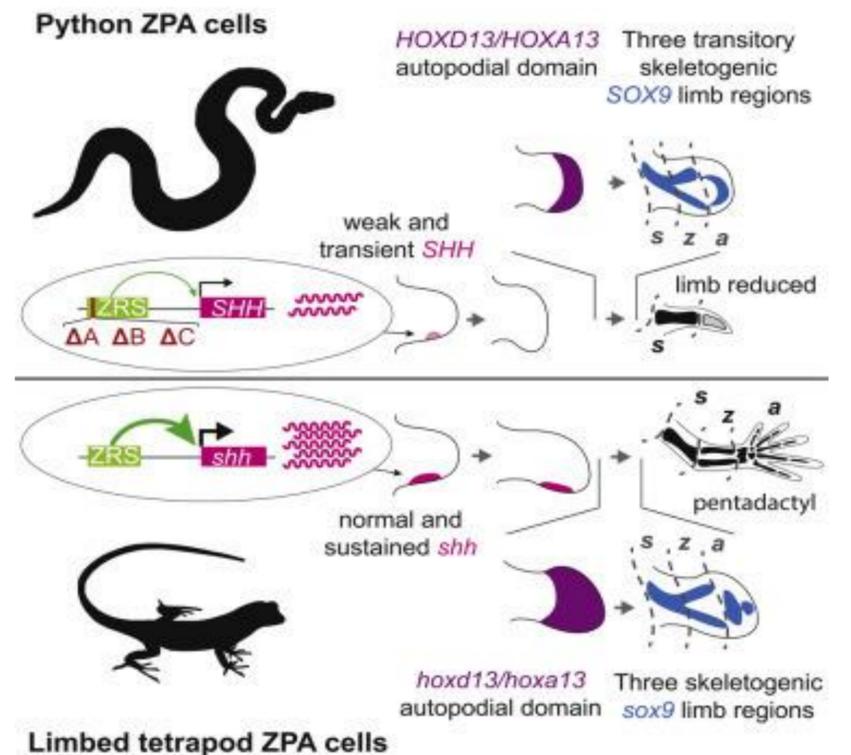


Figure 3: ZRS function results between similar animals (Reference 4)

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