

Scientists discover genomic key to plateau adaptation

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Hot-spring snake . Credit: ZHOU Zhengyan

Chinese scientists studying genomic data of hot-spring snakes have discovered the genetic mechanism for ectothermic animals' adaptation to extreme, high-elevation environments. The study, titled "Comparative

genomic investigation of high-elevation adaptation in ectothermic snakes," was published in *PNAS* on July 31.

Most animals have certain requirements for their living environment and have difficulty surviving if their environment is beyond the appropriate range. However, some [species](#) are able to survive and thrive under extreme conditions such as intense radiation or hypoxia; such species are called extreme environmental animals. Their long-term adaptive evolution makes these animals different from other organisms in terms of genetic structure, enzyme characteristics and metabolic function.

What is the hot-spring snake (Thermophis)?

The hot-spring snake belongs to the genus *Thermophis*, which currently includes three species: the hot-spring snake (*Thermophis baileyi*), the Sichuan hot-spring snake (*Thermophis zhaoermii*) and the Shangri-La hot-spring snake (*Thermophis Shangrila*). These rare species are protected in China and live in one of the world's highest habitats, the Qinghai-Tibet Plateau at an altitude ~3500-4400 meters above sea level. They mainly live in hot springs rock heaps, watersides and swamp meadows. The origin and evolution of hot spring snakes are closely related to the formation of the Qinghai-Tibet Plateau.

Why hot-spring snakes?

The Qinghai-Tibet Plateau is the highest and largest alpine region in the world. High elevation, a low growing season temperature, intense solar radiation and other factors related to the plateau's high-elevation environment have had a strong selective effect on speciation and population evolution. The region is a natural laboratory for studying the mechanisms of biological adaptation to the plateau environment.

"Previous studies mainly focused on the adaptation of homothermic animals to the plateau, but the [genetic mechanism](#) of ectothermic animals' adaptation to the plateau environment was still unknown," said LI Jiatang, a researcher from the Chengdu Institute of Biology of the Chinese Academy of Sciences and one of the first authors of the study.

The genetic mechanism for adaptation to extreme environments

The study found 27 unique amino acid replacements in 27 proteins of *Thermophis*. These mutations were predicted to impact function in the three species of *Thermophis*. "They were mainly associated with functions such as immunity, the adaptive response to hypoxia and DNA repair," said LI.

Molecular function experiments confirmed that mutation of the FEN1 (petal endonuclease-1) gene related to DNA damage repair was more stable under ultraviolet irradiation than the wild type (i.e., low-elevation species). Functional assays of the FEN1 alleles showed that the *Thermophis* allele is more stable under UV radiation than is the ancestral allele found in low-elevation species.

Mutation of the EPAS1 (endothelium PAS domain containing protein-1) gene of the hot-spring snake attenuates its ability to respond to hypoxia. Functional assays of EPAS1 alleles suggest that the *Thermophis* protein has lower transactivation activity than low-elevation forms. That is an important reason for the hot-spring [snake](#)'s adaptation to hypoxic conditions.

In response to national policies, more people have been working on the plateau in recent years. However, elevation sickness occurs frequently due to the high elevation. Research on the genetic mechanisms of

adaptation to the extreme [environment](#) of the [plateau](#) by homothermic animals and ectothermic animals will play a key role in the prevention and treatment of human high-elevation disease.

More information: Jia-Tang Li et al, Comparative genomic investigation of high-elevation adaptation in ectothermic snakes, *Proceedings of the National Academy of Sciences* (2018). [DOI: 10.1073/pnas.1805348115](#)

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