

Comparative genomic investigation of high-elevation adaptation in ectothermic snakes

With the support by the National Natural Science Foundation of China and the Chinese Academy of Sciences, the research team led by Prof. Li JiaTang (李家堂) at the CAS Key Laboratory of Mountain Ecological Restoration and Bioresource Utilization, Chengdu Institute of Biology, Chinese Academy of Sciences, explored the genetic mechanism of ectothermic animals' adaption to high-altitude extreme environments on the basis of genomic data of hot-spring snakes, which was published in *PNAS* (2018, 115 (33): 8406–8411).

The Qinghai-Tibet Plateau is the highest and largest alpine region in the world. High altitude, low growing season temperature, great intensity of solar radiation and other factors have been strong selective forces on the mechanism of speciation and population's evolution. Therefore, the Qinghai-Tibet Plateau is known as a natural laboratory for studying the mechanisms of biological adaptation to the plateau environment. Previous studies mainly focused on the adaptation of homothermic animals on the plateau, but the genetic mechanism of ectothermic animals' adaption to the plateau environment still remains unknown.

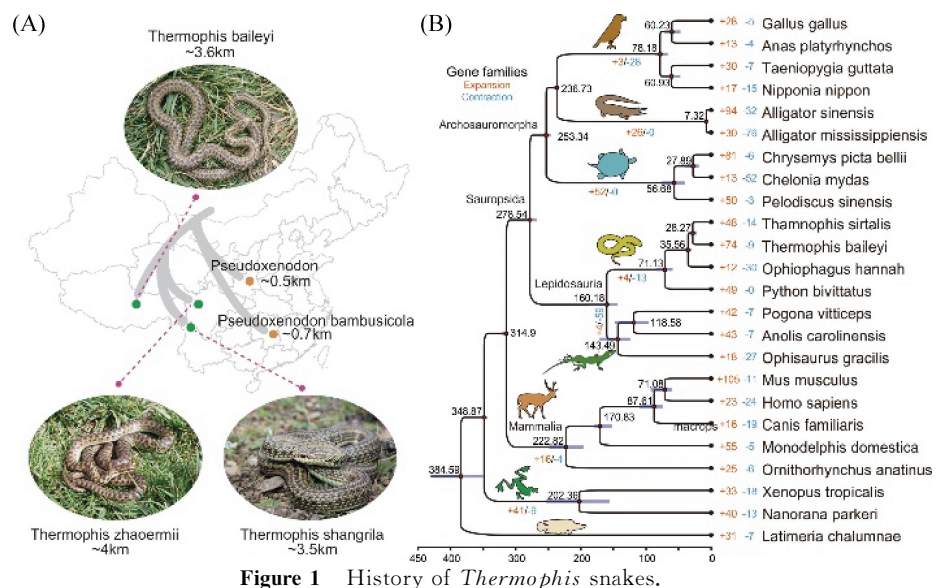


Figure 1 History of *Thermophis* snakes.

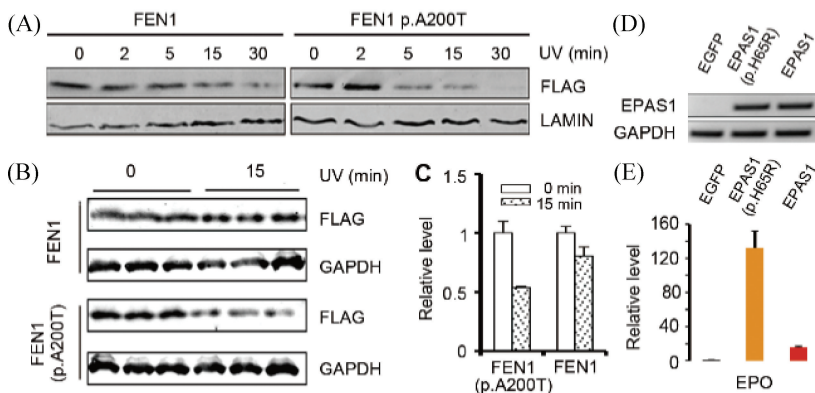


Figure 2 Functional assays of the FEN1 and EAPAS1 variantssshared by the high-elevation *Thermophis* snakes.

of the plateau, mutation of the EPAS1 (endothelium PAS domain containing protein-1) gene of the hot-spring snake attenuates its ability to regulate the expression of downstream gene erythropoietin, leading to a lower hemoglobin concentration. That is an important reason for the hot-spring snake's adaptation to high-altitude and low-oxygen conditions.

This study may promote research on the genetic mechanism of both homothermic and ectothermic animals' adaptation to the extreme environment of plateaux, which will play a substantial role in the prevention and treatment of human high altitude disease.

This study found that there were 27 substitutions of common amino acid in 27 different proteins in the three species of *Thermophis* and these mutations were mainly associated with functions such as immunity, hypoxia adaptive response and DNA repair. Molecular function experiments confirmed that the mutation of FEN1 (petal endonuclease-1) gene related to DNA repair was more stable under ultraviolet irradiation than the wild type (low-altitude species). It is speculated that the mutation contributes to the resistance of the *Thermophis* species to ultraviolet light in high altitude environments. As a species