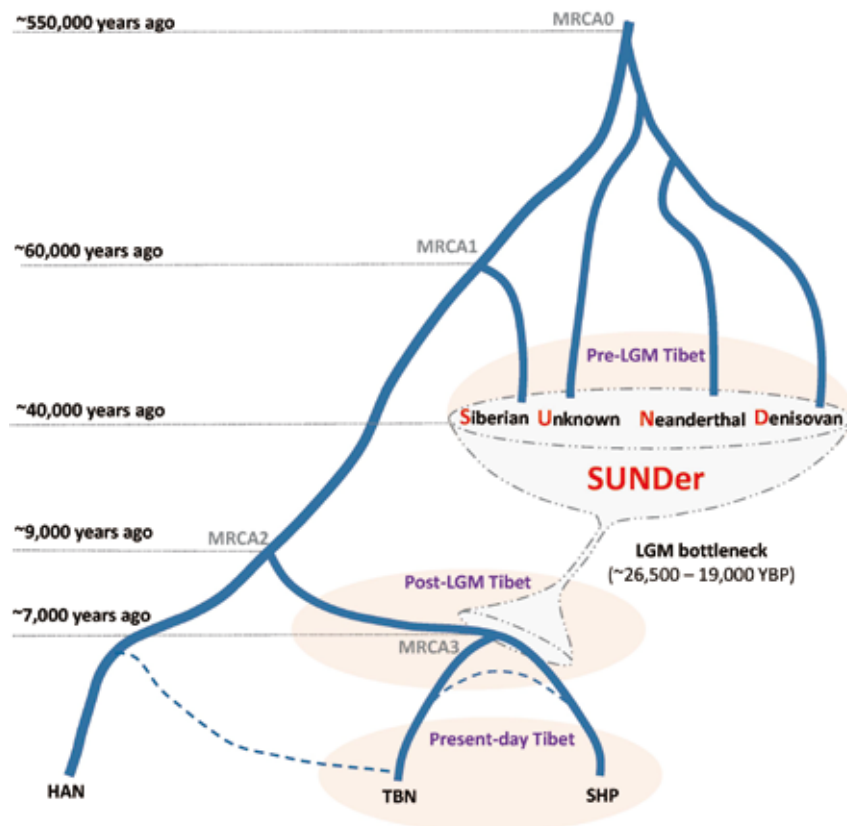


# Reconstruction of Genetic Origins and Population History of Tibetan Highlanders

Current knowledge of the origin and population history of Tibetan highlanders is still very much in its infancy and controversial. Who are the Tibetans? How long have they been living on the Tibetan Plateau, the “Roof of the World”? Who were the early highlanders? Were they modern human or non-modern human species? Whether is there a genetic continuity, or just some continuity of culture, between the pre-historical populations and present-day Tibetans? These

questions remain the most contentious puzzles in history, anthropology, and genetics.

A research team led by Dr. XU Shuhua from the CAS-MPG Partner Institute for Computational Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences analyzed deep-sequenced genomes of 38 Tibetan highlanders together with available data on archaic and modern humans, and comprehensively characterized the ancestral makeup of Tibetans and



**A sketch-map for the origins and demographic history of Tibetans and Sherpas.** A simplified model for the origins and evolutionary history of Tibetans and Sherpas based on the observations and estimations from this study. MRCA0: most recent common ancestor of modern human and archaic hominoids; MRCA1: most recent common ancestor of Eurasians; MRCA2: most recent common ancestor of HAN and TIB; MRCA3: most recent common ancestor of TBN and SHP. SUNDer: a tentative label for the early settlers who contributed ancient or archaic ancestry to present-day Tibetan highlanders. The two dashed lines connecting HAN and TBN, and TBN and SHP respectively represent possible gene flows occurred between populations. (Image provided by Dr. XU Shuhua's group)

unveiled their origins.

The researchers' analysis showed that Tibetans arose from a mixture of multiple ancestral gene pools, in particular, their analysis of ~200 contemporary populations showed that Tibetans share ancestry with populations from East Asia (~82%), Central Asia and Siberia (~11%), South Asia (~6%), and western Eurasia and Oceania (~1%). The Tibetans and Sherpas show closest affinities to the surrounding highland groups such as Yizu, Tu and Naxi, followed by lowland Han Chinese. The divergence time between Tibetan and Han Chinese populations was estimated to be ~15,000 to ~9,000 years ago.

The team not only adopted state-of-the-art methods but also developed a new method (ArchaicSeeker) to search for ancient ancestries in the genomes of Tibetan highlanders. They identified elevated archaic ancestry in Tibetans, and dated the most recent common ancestors of the surviving archaic lineages in the Tibetan genomes back to ~60,000–40,000 years ago, predating the Last Glacial Maximum (LGM). Their results indicate that plateau colonization and the altitudinal adaptation of human beings were considerably earlier and more complicated than previously suspected.

This study provides compelling evidence for the co-existence of both Paleolithic and Neolithic ancestries

on a genome-wide scale in the modern Tibetan gene pool, which supports a genetic continuity between pre-LGM highland-foragers and present-day Tibetans. The Paleolithic ancestries in the modern Tibetan gene pool, entangled with Denisovan-like, Neanderthal-like, ancient- Siberian-like, and unknown archaic sequences, indicate that Tibet remained a human melting pot where interbreeding occurred among different hominine groups before the LGM. The team suggested that the highly differentiated sequences harbored in highlanders' genomes were most likely inherited from pre-LGM settlers of multiple ancestral origins, a genetically admixed group which was named SUNDer and maintained in high frequency by natural selection. The team further proposed a two-wave "Admixture of Admixture" (AoA) model to help explain the ancestral make-up and pre-history of Tibetans and Sherpas.

Supported by the Strategic Priority Research Program of the Chinese Academy of Sciences, National Natural Science Foundation of China grants, and the Science and Technology Commission of Shanghai Municipality, the study entitled "Ancestral Origins and Genetic History of Tibetan Highlanders" was online published in *The American Journal of Human Genetics (AJHG)* on August 26, 2016.

