



Reconstruction of Y-chromosome phylogeny reveals two neolithic expansions of Tibeto-Burman populations

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Abstract

Diffusion of Tibeto-Burman populations across the Tibetan Plateau led to the largest human community in a high-altitude environment and has long been a focus of research on high-altitude adaptation, archeology, genetics, and linguistics. However, much uncertainty remains regarding the origin, diversification, and expansion of Tibeto-Burman populations. In this study, we analyzed a 7.0M bp region of 285 Y-chromosome sequences, including 81 newly reported ones, from male samples from Tibeto-Burman populations and other related Eastern Asian populations. We identified several paternal lineages specific to Tibeto-Burman populations, and most of these lineages emerged between 6000 and 2500 years ago. A phylogenetic tree and lineage dating both support the hypothesis that the establishment of Tibeto-Burman ancestral groups was triggered by Neolithic expansions from the middle Yellow River Basin and admixtures with local populations on the Tibetan Plateau who survived the Paleolithic Age. Furthermore, according to the geographical distributions of the haplogroups, we propose that there are two Neolithic expansion origins for all modern Tibeto-Burman populations. Our research provides a clear scenario about the sources, admixture process and later diffusion process of the ancestor population of all Tibeto-Burman populations.

Keywords Y-chromosome · Tibeto-Burman · Founder lineage · Tibetan Plateau

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Introduction

Tibeto-Burman populations are widely distributed in East Asia, Southeast Asia, and the northern part of South Asia. Tibeto-Burman populations on the Tibetan Plateau are the largest human communities that live in a high-altitude environment (Simons and Fennig 2017). Previous studies have

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provided some clues about the origin and gene pool of modern Tibeto-Burman populations (Shi et al. 2008; Zhang et al. 2017). However, the direct sources of the ancestor group, the diffusion process, and the specific paternal lineages of Tibeto-Burman populations remain ambiguous. This study aims to provide a clearer description of the origin and diffusion of Tibeto-Burman populations.

According to archeological findings, scholars have traced the common ancestors of current Sino-Tibetan populations to ancient populations of the early Yang-Shao culture (approximately 7000–6000 BP) in the upper-middle Yellow River basin (Sagart 2008; Van Driem 1999). Scholars have also postulated that the Ma-Jia-Yao culture (approximately 5400–4200 BP), derived from a western branch of the middle Yang-Shao culture, was created by ancestors of Proto-Tibeto-Burman populations (Sagart 2008; Van Driem 1999). The “Ma-Jia-Yao” culture was followed by the Qijia culture (4200–3800 BP), a Bronze Age culture with a flourishing jade ware tradition (Liu et al. 2010). The successors of the Qijia culture were the Kayue culture (3600–2700 BP), Xindian culture (3400–2600 BP), and Siwa culture (3300–2500 BP) (Ma et al. 2016). It is believed that these archeological cultures are related to modern Tibeto-Burman populations (An 1992). A recent archeological study demonstrated that permanent human occupation in the high-altitude area of the Tibetan Plateau occurred at approximately 3600 BP, after the establishment of sustained agriculture (Chen et al. 2015).

Previous studies provide clues to the origin and diffusion of Sino-Tibetan populations (Lu et al. 2016; Shi et al. 2008), as well as the factors that facilitated the motivation for expansion onto the Tibetan Plateau (Chen et al. 2015). Scholars have proposed that the ancient population on the plateau during the Paleolithic Age left genetic signals in the gene pool of current Tibeto-Burman populations, including Y-chromosome haplogroups D1-M15 and D3-P99 as well as the mtDNA haplogroups M16, M62, A10, and C4d (Qi et al. 2013, Su et al. 2000). According to Y-chromosome studies, sub-branches of haplogroups O3-M122 (Shi et al. 2005) and N-M231 are shared by all Han and Tibeto-Burman populations (Qi et al. 2013), indicating a second wave of migration during the early Neolithic, when farming and yak pastoralism were established on the plateau (Chen et al. 2015; Rhode et al. 2007). However, the initial differentiation pattern and the splitting time of the paternal lineage of Tibeto-Burman populations remain ambiguous.

Here, we analyzed the whole Y-chromosome sequences of 285 males from Tibeto-Burman populations and other related populations across East Asia and adjacent regions. We identified the founding paternal lineages for Tibeto-Burman populations. We characterized the initial differentiation of paternal lineages of Tibeto-Burman populations and explored the demographic history of Tibeto-Burman populations before their expansion across the Tibetan Plateau.

Methods

A detailed description of the methods can be found in SI Appendix, Materials and Methods. Briefly, blood samples from populations across China were collected from unrelated healthy males after obtaining informed consent. The ethics committee for biological research at the School of Life Sciences in Fudan University approved the study. Full genome sequencing and sequencing of target Y-chromosomes were performed using the Illumina HiSeq 2000 (San Diego, CA, USA). Mapping of reads and SNP (Single-nucleotide polymorphism) calling were conducted with the human reference hg37 using GATK packages and standard procedures for next-generation sequencing. Bayesian evolutionary analyses were implemented in BEAST (v1.8.0) (65). An age of 41,900 years for haplogroup NO (95% CI 40,175–43,359 years) was used for calibration (Karmin et al. 2015). To obtain a comprehensive overview of the paternal demographic history of East Asia populations, available Y-chromosome sequence data from publications were also included. In total, 285 sequences were analyzed, including 81 new sequences from our lab, the CAS-MPG team (Lu et al. 2016; Zhang et al. 2017) and the SGDP project (Mallick et al. 2016). All analyses in this study were conducted using reference hg19. We referred to <http://www.isogg.org> for the assignment of the SNP and haplogroup name. More detailed descriptions of sequence data processing, genotyping and filtering, the samples studied, phylogenetic inference, and dating are included in Additional files 4: Methods. The whole Y-chromosome sequences reported in this paper have been deposited in GenBank under accession number SRP136402.

Results

In total, Y-chromosome sequences of 285 males from our lab and previous publications were used to construct a phylogenetic tree (Fig. 1; Additional files 1: Figure S1; Additional files 2: Table S1). The revised phylogeny provided a clear resolution for the paternal genetic pool of Tibeto-Burman populations and other Eastern Asia populations. Based on the reconstructed phylogeny, many unique components were observed in Tibeto-Burman populations. In general, sub-lineages of haplogroup D-M174 and O2-M117-F5 (hereafter call O α -F5) are two predominant components in the paternal genetic pool of Tibeto-Burman populations.

Several sub-clades of haplogroup D-M174 were exclusively found in Tibeto-Burman populations, including D1a1a1a1a-F828, D1a1a1a2-Z31591, and D1a2a-P47

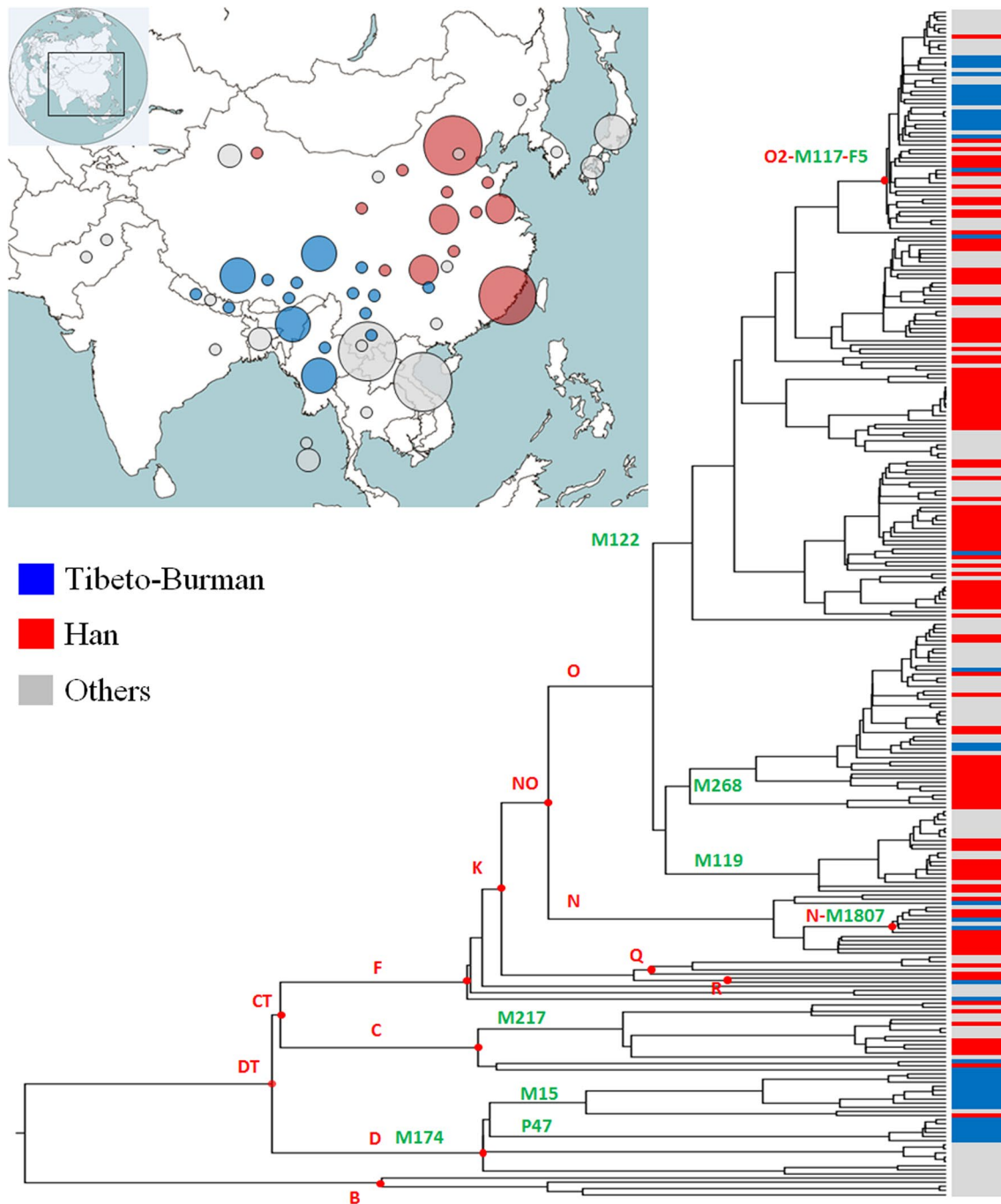


Fig. 1 Simplified phylogenetic tree showing sample locations. The size of the circle for each sampling location corresponds to the number of samples. See detailed information in Additional files 2: Table S1

(Fig. 1; Additional files 1: Figure S1; Additional files 2: Table S1). These three lineages separated from each other in the Paleolithic Age. However, the initial expansion of these three lineages occurred between 6000 and 5000 ybp (Additional files 3: Table S2). Interestingly, haplogroup D1a2-P47 separated from D1a1-M15 approximately 46 ky ago, whereas the most significant expansion of its

sub-clade, D1a2a1-PH116, only occurred ~2.5 ky ago. These results indicated that sub-clades of haplogroup D-M174 experienced an extreme long-term bottleneck effect before their expansion in the past several thousand years.

Most of the samples of O-F5 from Tibeto-Burman populations belonged to the sub-branch O1 α 1c1-CTS1642

(5809 years ago, 95% CI 5301–6427 years ago) (Fig. 1; Additional files 1: Figure S1; Additional files 2: Table S1; Additional files 3: Table S2). Haplogroup O1α1c1-CTS1642 is composed of two specific sub-lineages, Oα1c1a-Z25929 (5555 years, 95% CI 5015–6118 years) and Oα1c1b-CTS5308 (5199 years, 95% CI 4625–5794 years). Samples of Oα1c1b-CTS5308 were mainly found in Tibetan, Sherpa, Riang and Dai populations (Additional files 1: Figure S1; Additional files 2: Table S1). These populations mainly came from the Tibetan Plateau and adjacent regions. One Han population sample also belonged to this lineage. In addition, the ~2400-year-old ancient remains Chokhopani-C1 from Nepal (Jeong et al. 2016) and modern sample bhu-1554 from Bhutan (Hallast et al. 2015) also belong to Oα1c1b-CTS5308. On the other hand, samples of Oα1c1a-Z25929 were found from Yi (HGDP01186), Burmese, Naxi, Jingpo, Riang, Tibetan, Bangladeshi, Dai, Han, and Kinh populations (Additional files 1: Figure S1; Additional files 2: Table S1). These populations mainly come from the Yunnan province of China, Burma and the North-east part of South Asia. Although there are some exceptions, the geographic distributions of Oα1c1a-Z25929 and Oα1c1b-CTS5308 are generally distinct from each other.

Interestingly, most Oα-F5 samples from Dai, a Daic population in Yunnan, belong to the specific sub-lineage Oα1c1a1a-Y7080, which emerged only ~2000 years ago (Additional files 1: Figure S1; Additional files 3: Table S2). Given that most other sub-branches of Oα1c1a-Z25929 came from Tibeto-Burman populations, Oα1c1a1a-Y7080 may represent recent admixture from Tibeto-Burman populations into the Dai population. A similar scenario was discovered in a genome-wide study that showed that the populations in the Tibetan-Yi Corridor are admixed, deriving ancestry from Tibetan highlanders and surrounding lowland East Asians approximately 150–2100 years ago (Yao et al. 2017). Samples of other paternal lineages only contributed to a minor percent of the paternal gene pool of Tibeto-Burman populations. Therefore, these lineages are likely the results of ancient or recent admixture from surrounding populations during the expansion of Tibeto-Burman populations.

We constructed Bayesian skyline plots to analyze effective population sizes over time for the Tibeto-Burman and Han Chinese populations (Fig. 2). Obvious differences were observed between the two skyline plots. For Tibeto-Burman populations, an increase in population size occurred in the Paleolithic Age more than 40,000 years ago, indicating the initial peopling of the Tibetan Plateau (Fig. 2b). Afterwards, a period of relative stability lasted for tens of thousands of years before a rapid expansion occurred in the Neolithic Age, probably due to the difficult survival with insufficient food resources on the Plateau during the Paleolithic Age. By contrast, continuous population growth of samples from Han Chinese populations since the Paleolithic Age was observed

(Fig. 2a). Between 11 and 6 kya, the ancestor group of Han populations experienced exponential growth, while a significant decrease in population was observed for the ancestor group of Tibeto-Burman populations. Later, however, the expansion of Tibeto-Burman populations and Han populations after the Neolithic Demographic Transition period (after 6 kya) seems to be synchronous to some degree. However, a previous study demonstrated that population substructure, genetic barriers, limited sampling locations, and isolation of panmixia impact the BSP analysis and can cause bias by producing spurious signals for population size change (Heller et al. 2013). A previous study indeed found a strong population substructure in Sherpa and Tibetan populations (Zhang et al. 2017). Therefore, the decrease in population predicted by BSP analysis of Tibeto-Burman populations should be treated with caution. More sampling and further analyses are needed to reveal the complex population structure in all Tibeto-Burman populations in the future.

Discussion

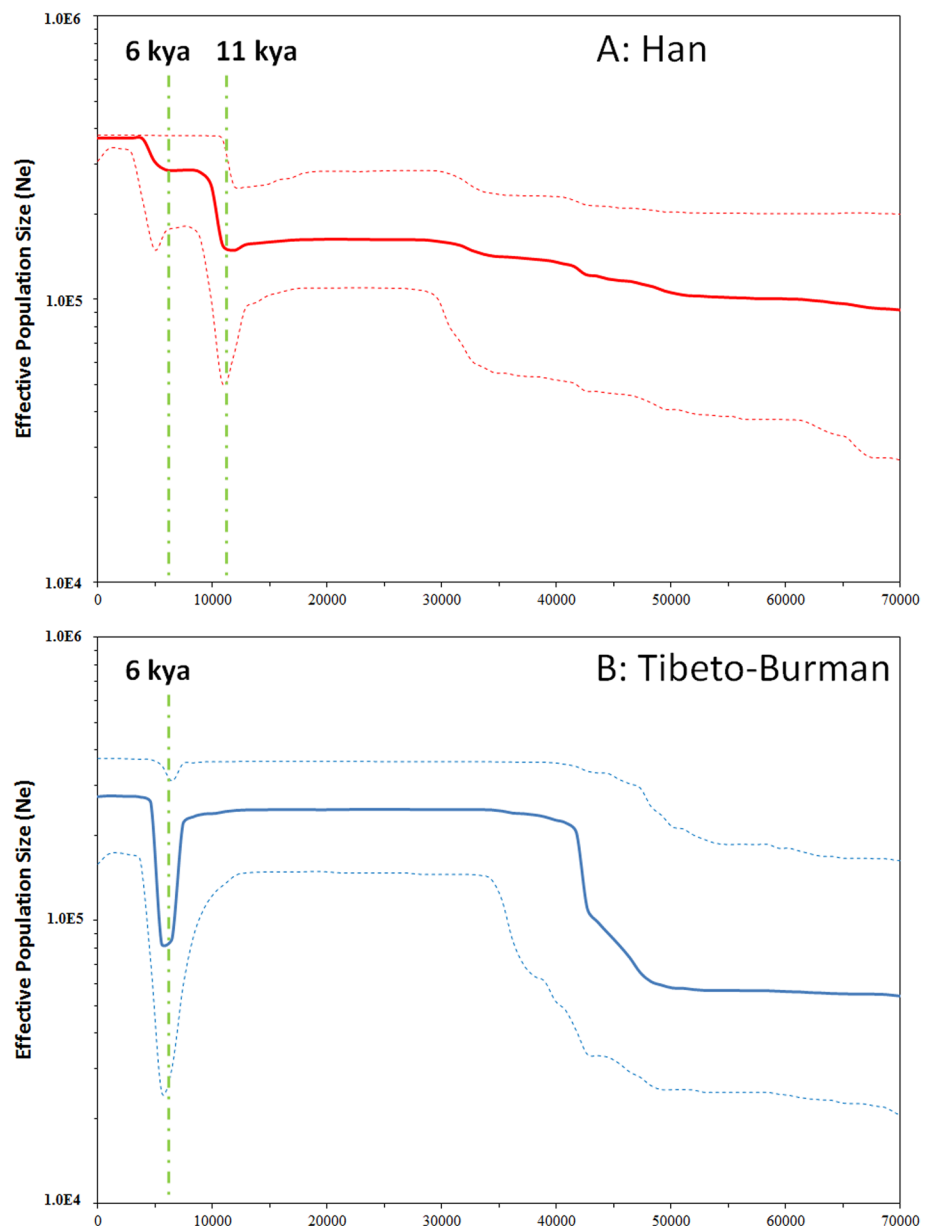
Founding paternal lineages of Tibeto-Burman populations

According to previous research and the results of this study, we propose that Oα1c1b-CTS5308, Oα1c1a-Z25929 and various sub-lineages of D-M174 are the founding paternal lineages of Tibeto-Burman populations. The initial expansion times of all these founding lineages fall into a short period between 6 and 5 ky ago (Additional files 3: Table S2).

Most scholars believe that haplogroup D-M174 represents the relics of the initial peopling of modern humans on the Tibetan Plateau, which may have survived during the Last Glacial Maximum (Qi et al. 2013; Shi et al. 2008; Su et al. 2000). Our estimate indicated that D1b-M46.1, D1a1-M15, and D1a2-P47 separated from each other at ~46 kya (Additional files 3: Table S2). However, the expansion time of sub-lineages of D1a1-M15 and D1a2-P47 in Tibeto-Burman populations occurred ~6 kya, after the appearance of the Laoguantai Culture (~7800–7000 BP) and Yang-Shao culture (~7000–5500 BP), two early Neolithic cultures in the upper-middle Yellow River basin (Additional files 3: Table S2). Therefore, the phylogenetic tree, age estimates and skyline plots suggest that ancestor group of Tibeto-Burman populations with paternal lineages D1a1-M15 and D1a2-P47 experienced a long-term bottleneck effect that lasted for tens of thousands of years before their expansion in the Neolithic Age.

Most importantly, the age of the most recent common ancestor of Oα1c1b-CTS5308 (~5200 years ago) and Oα1c1a-Z25929 (~5550 years ago) is surprisingly close to the age of the Majiayao culture (~5400–4900 BP).

Fig. 2 Bayesian skyline plots of effective population size for Han and Tibeto-Burman populations



Archeological studies suggest that a subgroup of ancient populations of the Miaodigou culture (~ 6300–5500 BP) moved westward to the upper stream region of the Yellow River and created the Majiayao culture (~ 5400–4900 BP) (Liu et al. 2010), which was proposed to be the remains of direct ancestors of Tibeto-Burman populations (Sagart 2008). On the other hand, Han populations, the other major descendant group of the Yang-Shao culture (~ 7000–5500 BP), are composed of many other sub-lineages of O α -F5 and extremely low frequencies of D-M174 (Additional files 1: Figure S1; Additional files 2: Table S1). Therefore, we propose that O α -F5 may be one of the dominant paternal lineages in ancient populations of Yang-Shao culture and its successors.

In this study, we demonstrated that both sub-lineages of D-M174 and O α -F5 are founding paternal lineages of modern Tibeto-Burman populations. The genetic patterns suggested that the ancestor group of modern Tibeto-Burman populations may be an admixture of two distinct ancient populations. One of them may be hunter-gatherer populations who survived on the plateau since the Paleolithic Age, represented by varied sub-lineages of sub-lineages of D-M174. The other one was comprised of farmers who migrated from the middle Yellow River basin, represented by sub-lineages of O α -F5. In general, the genetic evidence in this study supports the conclusion that the appearance of the ancestor group of Tibeto-Burman populations was triggered by the Neolithic expansion from the upper-middle

Yellow River basin and admixture with local populations on the Tibetan Plateau (Su et al. 2000).

Two neolithic expansion origins of Tibeto-Burman populations

We also observed significant differences in the paternal gene pool of different subgroups of Tibeto-Burman populations. Haplogroup D-M174 contributed ~54% percent in a sampling of 2354 Tibetan males throughout the Tibetan Plateau (Qi et al. 2013). Previous studies have also found high frequencies of D-M174 in other populations on the Tibetan Plateau (Shi et al. 2008), including Sherpa (Lu et al. 2016) and Qiang (Wang et al. 2014). In contrast, haplogroup D-M174 is rare or absent from Tibeto-Burman populations from Northeast India and Burma (Shi et al. 2008). In populations of the Ngwi-Burmese language subgroup, the average frequencies of haplogroup D-M174 are ~5% (Dong et al. 2004; Peng et al. 2014). Furthermore, we found that lineage O α 1c1b-CTS5308 is mainly found in Tibeto-Burman populations from the Tibetan Plateau. In contrast, lineage O α 1c1a-Z25929 was found in Tibeto-Burman populations from Northeast India, Burma, and the Yunnan and Hunan provinces of China (Additional files 1: Figure S1; Additional files 2: Table S1). In general, enrichment of lineage O α 1c1b-CTS5308 and high frequencies of D-M174 can be found in

most Tibeto-Burman populations on the Tibetan Plateau and adjacent regions, whereas Tibeto-Burman populations from other regions tend to have lineage O α 1c1a-Z25929 and a little to no percentage of D-M174.

The inconsistent pattern we observed in the paternal gene pool of modern Tibeto-Burman populations suggested that there may be two distinct ancestor groups (Fig. 3). The proposed migration routes shown in Fig. 3 are somewhat different from those proposed by Su et al. (2000). According to our age estimation, most of the D1a2a-P47 samples belong to sub-lineage PH116, a young lineage that emerged ~2500 years ago (95% CI 1915–3188 years). On the other hand, continuous differentiation can be observed on a phylogenetic tree of lineages D1a1a1a1-PH4979 and D1a1a1a2-Z31591 since 6000 years ago. Therefore, we proposed that a group of ancient populations may have moved to the upper basin of the Yellow River and admixed intensively with local populations with high frequencies of haplogroup D-M174, including its sub-lineage D1a2a-P47 (Fig. 3). This ancestor group eventually gave birth to modern Tibeto-Burman populations on the Tibetan Plateau and adjacent regions. The other ancestor group moved toward the southwest and finally reached South East Asia (Burma and other locations) and the northeastern part of India (Fig. 3). This ancestor group may have had no or a minor admixture of D-M174 in their paternal gene pool.

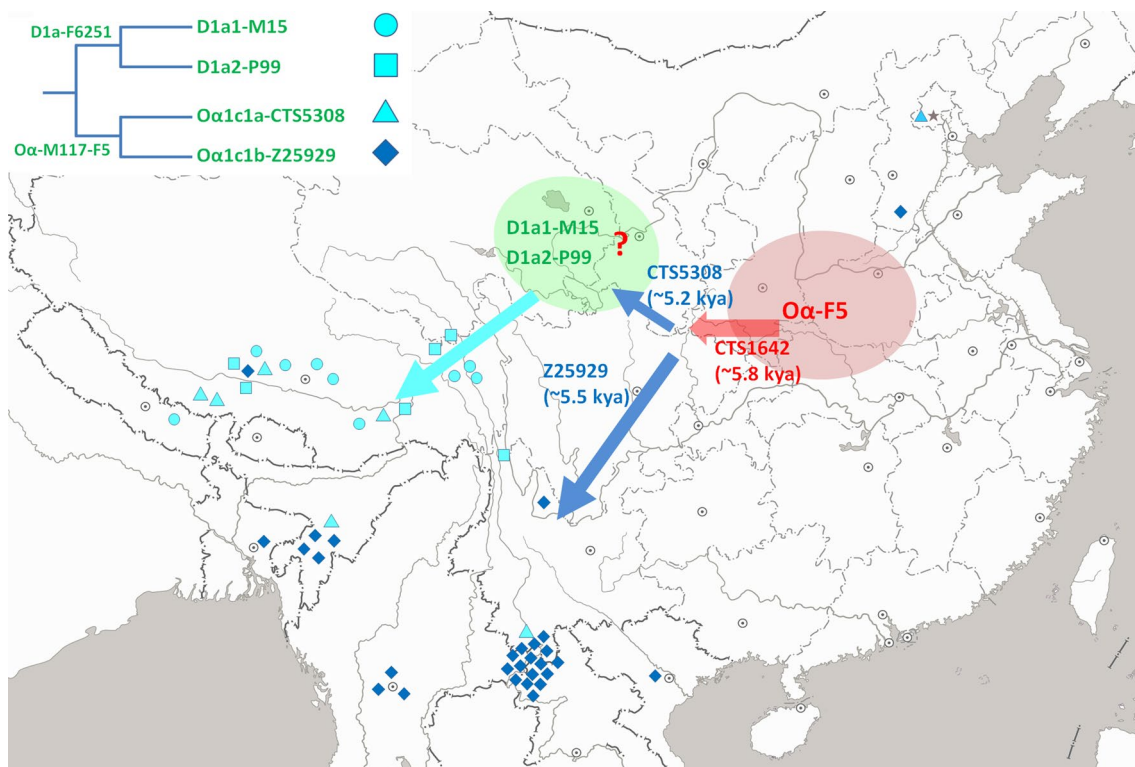


Fig. 3 Two proposed ancestor groups and migration routes for Tibeto-Burman populations

Long-term admixture before expansion to a high-altitude region

It is interesting to investigate the time gap between the appearance of Neolithic cultures in the northeastern part of the Tibetan Plateau and the final phase of human expansion across the Tibetan Plateau. The Majiayao culture (~5400–4900 BP) is the earliest Neolithic culture in the northeastern part of the Tibetan Plateau (Liu et al. 2010). However, previous archeological study has suggested that the final phase of diffusion into the high-altitude area of the Tibetan Plateau occurred at approximately 3.6 kya (Chen et al. 2015). Our genetic evidence in this study is consistent with this scenario based on archeological evidence. Based on Y-chromosome analysis in this study, many unique lineages of Tibeto-Burman populations emerged between 6000 years ago and 2500 years ago (Additional files 3: Table S2). The most recent common age of D1a2-PH116, a sub-lineage that spread throughout the Tibetan Plateau, is only 2500 years ago.

We propose that there may be two important factors for the observed age gap. First, living in a high-altitude environment may require some crucial physical characteristics that were lacking from Neolithic immigrants from the middle Yellow River Basin. Intense genetic admixture with local people who had survived on the Tibetan Plateau since the Paleolithic Age may have actually guaranteed the expansion of humans across the Tibetan Plateau. Therefore, a long period of admixture, lasting from 5.4 to 3.6 kya, may be necessary for the appearance of a population with beneficial genetic variants that was genetically adapted to the high-altitude environment. Second, technological innovations, such as the domestication of wheat and highland barley (Chen et al. 2015), establishment of yak pastoralism (Rhode et al. 2007), and introduction of other culture elements in the Bronze Age (Ma et al. 2016), are also important factors that facilitated permanent settlements with large population sizes in the high-altitude area of the Tibetan Plateau.

In summary, we constructed a high-resolution phylogeny of paternal lineages of Tibeto-Burman populations and identified several founding paternal lineages. We demonstrated that the ancestor groups of modern Tibeto-Burman populations may be the results of admixture between local populations on the Plateau and Neolithic immigrants from the middle Yellow River Basin. Furthermore, we propose that the current significant difference in the phylogeographical distribution of modern Tibeto-Burman populations is mainly due to two distinct ancestral groups of Neolithic expansions. The long-term genetic admixture after the appearance of earliest Neolithic culture in northeast part of the Tibetan Plateau may have guaranteed the physical adaptation of modern humans to this high-altitude environment. The findings in this study are crucial for understanding the demographic

background of the emergent Tibeto-Burman population as well as its diffusion across the Tibetan Plateau. Our results show that whole Y-chromosome sequencing is a powerful tool to investigate the origin and differentiation history of a group of populations. Further analysis of the founder paternal lineages found in this study and samples from additional populations are needed to study the differentiation of sub-branches of Tibeto-Burman populations, the complicated demographic history on the plateau, and the epic migration across the Himalayas.

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Author contribution LXW, YL, CZ, and LHW carried out the molecular genetic studies and drafted the manuscript. YL, CZ, SHX, SY, and SM collected the samples. YL, CZ, and SY participated in the experiments. YZH, CCW, SQW, SM, and LJ participated in the statistical analysis. SHX and HL designed the study and revised the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Research involving human participants and/or animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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