

Genome-wide analysis reveals population structure and selection in Chinese indigenous sheep breeds and reveals adaptation to high-altitude hypoxia in Tibetan sheep

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Traditionally, Chinese indigenous sheep were classified geographically and morphologically into three groups: Mongolian, Kazakh and Tibetan. Herein, we evaluate the population structure and genome selection among 140 individuals from ten representative Chinese indigenous sheep breeds: Ujimqin, Hu, Tong, Large-Tailed Han and Lop breed (Mongolian group); Duolang and Kazakh (Kazakh group); and Diqing, Plateau-type Tibetan, and Valley-type Tibetan breed (Tibetan group). We analyzed the population structure using principal component analysis (PCA), STRUCTURE and a Neighbor-Joining (NJ)-tree. In PCA plot, the Tibetan and Mongolian groups were clustered as expected; however, Duolang and Kazakh (Kazakh group) were segregated. STRUCTURE analyses suggested two subpopulations: one from North China (Kazakh and Mongolian groups) and the other from the Southwest (Tibetan group). In the NJ-tree, the Tibetan group formed an independent branch and the Kazakh and Mongolian groups were mixed. We then used the di statistic approach to reveal selection in Chinese indigenous sheep breeds. Among the 599 genome sequence windows analyzed, 16 (2.7%) exhibited signatures of selection in four or more breeds. We detected three strong selection windows involving three functional genes: *RXFP2*, *PPP1CC* and *PDGFD*. *PDGFD*, one of the four subfamilies of PDGE, which promotes proliferation and inhibits differentiation of preadipocytes, was significantly selected in fat type breeds by the Rsb (across pairs of populations) approach. Two consecutive selection regions in Duolang sheep were obviously different to other breeds. One region was in OAR2 including three genes (*NPR2*, *SPAG8* and *HINT2*) the influence growth traits. The other region was in OAR 6 including four genes (*PKD2*, *SPP1*, *MEPE*, and *IBSP*) associated with a milk production quantitative trait locus. We also identified known candidate genes such as *BMPR1B*, *MSRB3*, and three genes (*KIT*, *MC1R*, and *FRY*) that influence lambing percentage, ear size and coat phenotypes, respectively. Tibetan sheep have lived at Tibetan plateau for thousands of years. They have adapted to the extreme environment of high altitude hypoxia through a long period of natural selection. Seven sheep breeds, can be clustered highland and lowland respectively, living at different area of China. FST and XP-EHH approaches were used to identify the regions harboring local positive selection between these two groups. We found 171 SNPs containing 152 genes with signals of positive selection in the highland sheep, with 21 of these candidate genes as being associated with high-altitude adaptation. Such as *EPAS1*, *NF1*, *LONP1*, *DPP4*, *SOD1*, *PPARG*, *SOCS2* are involved in responses to hypoxia. Mutations of twelve are identified in exons at *EPAS1*, especially, one of which happened to a quite conserved site in the *EPAS1* 3'UTR domain. The relationship between blood-related phenotypes and *EPAS1* genotypes on additional highland sheep at this loci reveals that the homozygous mutation is associated with the improved mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular volume (MCV), which may help us to better understand physiological adaptability on Tibetan sheep. Taken together, our results not only provide the evidence on the genetic diversity of the highland sheep but also suggest potential mechanism for adaptation to hypoxia of high-altitude as well as the role of *EPAS1* in the adaptive processes.

Biography

Caihong Wei has completed his PhD from Gansu Agricultrural University. She is a key specialist of National Mutton Sheep Industry Technology System, a associated research fellow and a master tutor at the Chinese Academy of Agricultural Sciences (CAAS). She has published more than 16 papers in reputed journals and two monographs.

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