



Association of novel single-nucleotide polymorphisms of the vascular endothelial growth factor-A gene with high-altitude adaptation in yak (*Bos grunniens*)

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ABSTRACT. Vascular endothelial growth factor-A gene (*VEGF-A*) is a key regulator of angiogenesis and an endothelial cell mitogen that plays an important role in high-altitude adaptation. In this study, we detected 2 novel single-nucleotide polymorphisms (SNPs) of *VEGF-A* by screening for genetic variation in 700 individuals of 3 domestic Chinese yak breeds - namely Gannan (GN), Datong (DT), and Tianzhu white (TZW) - using polymerase chain reaction-restriction fragment length polymorphism and DNA sequencing techniques. GN and DT yaks live at high altitude and TZW yaks live at low altitude on the Qinghai-Tibetan Plateau. SNP g.8430T>C is located in intron 4 of *VEGF-A*. SNP g.14853G>A is located in the 3' untranslated region of *VEGF-A*. Frequencies of the GA and AA genotypes and the A allele of SNP g.14853G>A observed in GN and DT yaks were significantly higher than that in TZW yaks ($P < 0.01$). No significant difference among the breeds was observed for SNP g.8430T>C. The frequency

of haplotype TA was significantly higher ($P < 0.01$), whereas the frequency of TG ($P < 0.01$) was significantly lower in GN and DT yaks compared with that in TZW yaks. The 2 SNPs were in moderate linkage disequilibrium in GN and DT yaks, but not in TZW yaks. The fixation index (F_{ST}) pairwise value was significantly different among the breeds studied. The neutral test result indicated that the region between the 2 SNPs may have been subjected to positive or balancing selection, and the high-altitude hypoxia environment might be the main determinant for selection. These results suggest that *VEGF-A* might contribute to the high-altitude adaptability of yak.

Key words: Vascular endothelial growth factor A (VEGF-A); Polymorphism; High-altitude adaptation; Hypoxia adaptation; Yak