Population Genetics, Genetic Epidemiology, Statistics, Bioinformatics

AB007. Search of signals for cold adaptation in native populations of Siberia by whole exome sequencing

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Background: Adaptation to cold climate, mediated by natural selection has played the substantial role in shaping the genetic and phenotypic structure of human populations settled in Siberia and North Asia. Goal of this work was to characterize the portion of genetic diversity in coding regions of the genome in native Siberian and North Asian populations, potentially adaptive for cold climate conditions.

Methods: Whole exome sequencing using Illumina HiSeq 2000 platform was performed in pilot population samples from four native Siberian and North Asian populations: Khants, Kets, Yakuts and Evenki. Bioinformatic analysis was focused on the search for population-specific variants, which are characterized by functional significance and belong to genes involved in functions and processes related to cold adaptation.

Results: Number of SNPs and InDels in individual exome ranged from 40,556 to 43,471 and from 3,983 to 4,530 respectively. Each exome bears around 8.5 K missense and 230 nonsense mutations. Data filtering for functionally significant variants (characterized by high or moderate impact by multiple functional predictions algorithms) not present or rare (MAF <0.05) in 1,000 Genomes Asian population resulted in 339 variants fixed or very common in all four Siberian samples. Analysis of this subset for functional pathways and candidate genes associated with cold adaptation reveals 18 functional variants fixed at least in 1 of 4 Siberian populations and very common in others. These variants include genetic variation in coding regions of genes involved in smooth muscle contraction, non-shivering thermogenesis, blood pressure regulation, response to temperature, base metabolism rate and others pathways.

Conclusions: We suggest that accumulation of fixed coding variants in genes involved in metabolism regulation, energy production and smooth muscle contraction reflects the positive selection for cold adaptation in native Siberians.

Keywords: Siberia; North Asia; adaptation; positive selection; exome sequencing