RESEARCH**SNAPSHOT**

School of Education exercise science professor Tom Brutsaert (left) and doctoral student Jason Howard stand above Cerro de Pasco, Peru, the world's highest altitude city (14,370 feet) with a population of more than 50,000 people.

PROJECT: Natural selection and genes determining higher arterial saturation in Peruvian Quechua

INVESTIGATOR: Tom Brutsaert

DEPARTMENT: Exercise Science

SPONSOR: National Science Foundation

AWARD AMOUNT: $346,384 (September 2011-August 2014)

BACKGROUND: Human populations in both the Andes and Himalaya have resided at high altitude for millennia and may have experienced natural selection in response to hypoxia, a condition in which the body's oxygen supply is depleted at a high altitude. Recent studies indicate this was almost certainly the case among Tibetan natives in the Himalaya, and several genes have been identified that help explain the tolerance of Tibetans to high altitude. Similar compelling evidence does not exist for indigenous populations in South America, despite a similar time frame of residence in the highlands. However, this research has identified several promising genetic loci in the indigenous Peruvian Quechua that show a priori evidence of natural selection and are associated with a higher arterial oxygen saturation during exercise. The arterial oxygen saturation is a particularly promising trait for genetic analysis as it is the major determinant of the overall oxygen-carrying capacity of the blood. The Peru project's goal is to collect physiological and genetic data (DNA) sufficient to support studies at the genome-wide level, and sufficient to test hypotheses of Quechua evolutionary adaptation to life at high altitude. The research team is collecting many samples in the city of Cerro de Pasco, Peru (approximately 14,300 feet above sea level), the world's highest altitude city with a population of more than 50,000 inhabitants. The majority of these inhabitants have deep Quechua ancestry.

IMPACT: Little is known regarding the genetic basis and population distribution of alleles (genes) that influence the oxygen transport system. As stated, the research group has identified several promising genetic markers in Quechua. If these results can be confirmed, the longer-term results of this project could add significantly to understanding human adaptation to high altitude, as well as shed light on variants controlling a number of complex phenotypes. When complete, the DNA samples and the physiological data collected in this study will comprise the largest and most comprehensive "genotype-phenotype" sample of highland natives in the world. Thus, the data are intended to support future genome-wide and fine-mapping studies that will have the goal of identifying the causal genetic variants that explain the unique adaptive features of highland natives in South America.