

New fruit fly research pinpoints genomic hallmarks of human high altitude adaptation

November 17 2015

21 percent. That's the amount of oxygen in the air that we breathe—with the exception of the extreme high-altitude dwellers on the Tibetan or Andean mountains.

To get at the genetic roots of these thin air thrivers, a collaborative research team led by Kevin White and Gabriel Haddad of University of Chicago and UC San Diego respectively, turned to a research workhorse, the fruit fly and identified a treasure trove of new genes—all told, over 100 genes that may be critical to high-altitude adaptation, with more than 40 similar genes found in humans. The results were published in the advanced online edition of *Molecular Biology and Evolution*.

Using experimental evolution followed by whole genome sequencing (dubbed "evolve and re-sequence"), the research team grew three fruit fly populations under severely hypoxic conditions over many generations. Sequencing the hypoxia-tolerant flies (surviving on just 5 percent oxygen by the 13th generation) they identified 3,800 single mutations many of which mapped within 66 genomic regions and prioritized a total of 99 candidate fruit fly genes. Many of these were primarily associated with development of respiratory system in [fruit flies](#). In addition, gene knockdown experiments of the targets significantly enhanced survival under severe [hypoxic conditions](#). "In a tribute to legendary Sherpa mountaineers of Nepal, we named three of the previously unnamed fruit fly genes implicated in metabolic rewiring as Pasang Lhamu, Tenzing Norgay and Phurba Tashi," said Aashish Jha, a graduate student in Kevin White's lab and the first author of the study.

When the research team examined similar genes in high-altitude populations, they found several single mutation differences between high-altitude human populations and their lowland neighbors.

Human comparative data from Andeans (n=10), Sherpas (69) Tibetans (96) and Ethiopian highlanders (165) showed that of the 102 human genes that are similar to the 55 hypoxia genes in fruit fly, more than 40 appear to enable hypoxia tolerance in Sherpas, Tibetans and Ethiopian highlanders. A smaller number (n=21) of genes were shared in the Andean population, which may have been due to the small sample size (just 10 individuals). Prof. White explains, "These results show that, to our surprise, genetic variation in the same types of [genes](#) can produce hypoxia resistance in both humans and fruit flies. This result implies that even across hundreds of millions years of evolution, organisms can arrive at convergent solutions during adaptation to similar types of environmental change."

Provided by Oxford University Press

Citation: New fruit fly research pinpoints genomic hallmarks of human high altitude adaptation (2015, November 17) retrieved 4 May 2024 from <https://phys.org/news/2015-11-fruit-genomic-hallmarks-human-high.html>

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