A Selective Sweep on a Deleterious Mutation in CPT1A in Arctic Populations

Arctic populations live in an environment characterized by extreme cold and the absence of plant foods for much of the year and are likely to have undergone genetic adaptations to these environmental conditions in the time they have been living there. Genome-wide selection scans based on genotype data from native Siberians have previously highlighted a 3 Mb chromosome 11 region containing 79 protein-coding genes as the strongest candidates for positive selection in Northeast Siberians. However, it was not possible to determine which of the genes might be driving the selection signal. Here, using whole-genome high-coverage sequence data, we identified the most likely causative variant as a nonsynonymous G>A transition (rs80356779; c.1436C>T [p.Pro479Leu] on the reverse strand) in CPT1A, a key regulator of mitochondrial long-chain fatty-acid oxidation. Remarkably, the derived allele is associated with hypoketotic hypoglycemia and high infant mortality yet occurs at high frequency in Canadian and Greenland Inuits and was also found at 68% frequency in our Northeast Siberian sample. We provide evidence of one of the strongest selective sweeps reported in humans; this sweep has driven this variant to high frequency in circum-Arctic populations within the last 6–23 ka despite associated deleterious consequences, possibly as a result of the selective advantage it originally provided to either a high-fat diet or a cold environment.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Metagenomics, University of Cambridge, University of California at Berkeley, University of Bristol, Liverpool School of Tropical Medicine, University of Tartu, University of Southampton
Pages: 584–589
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: American Journal of Human Genetics
Volume: 95
Issue number: 5
ISSN (Print): 0002-9297
Ratings:
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 8.34 SJR 7.45 SNIP 2.428
Web of Science (2017): Impact factor 8.855
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.43 SJR 7.504 SNIP 2.536
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 9.71 SJR 8.755 SNIP 3.01
Web of Science (2015): Impact factor 10.794
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 9.66 SJR 8.801 SNIP 3.195
Web of Science (2014): Impact factor 10.931
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 9.58 SJR 7.863 SNIP 3.039
Web of Science (2013): Impact factor 10.987
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 9.86 SJR 7.814 SNIP 3.06