Adaptive fitness advantage in ancestors: a major health risk to a present-day Arab population

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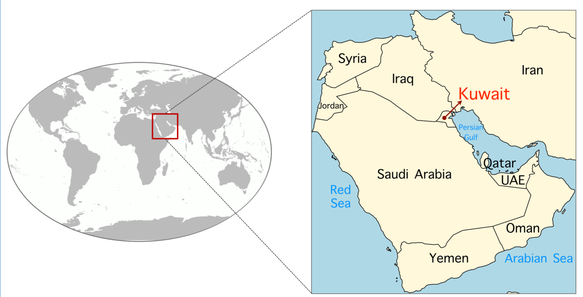
BACKGROUND

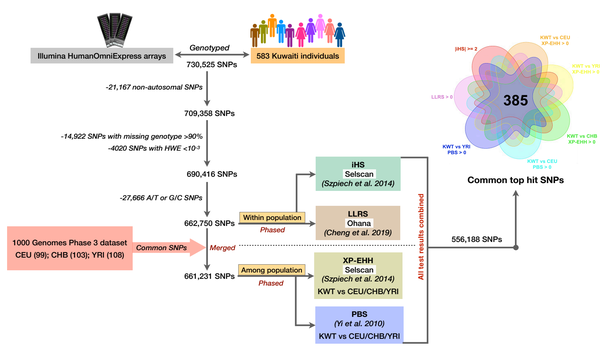
Following the out-of-Africa diaspora, the Arabian Peninsula (AP) has experienced several waves of human migrations despite the prevailing extreme and varying environmental conditions. The potential adaptation that shaped the extant human populations of the hot and dry environment of the Arabian Peninsula have been scarcely studied.



Geographic location of the genotyped individuals from the State of Kuwait in the Arabian Peninsula

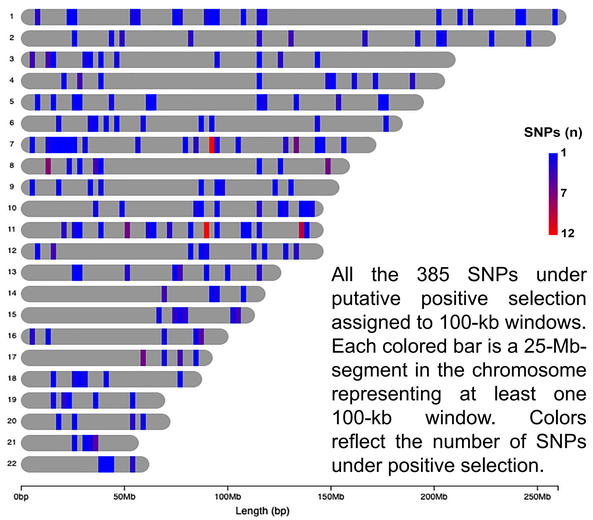
METHODS

To explore natural selection in the AP region, we analyzed 662,750 variants in 583 Kuwaiti individuals applying multiple statistical tests:
(i) integrated Haplotype Score (iHS)
(ii) Cross Population Extended Haplotype Homozygosity (XP-EHH)
(iii) Population Branch Statistics (PBS)
(iv) log-likelihood ratio scores (LLRS)



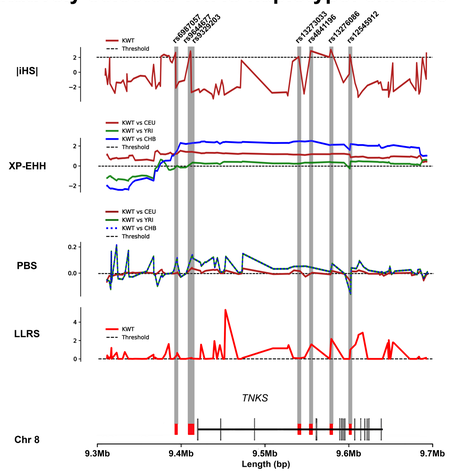
RESULTS

(1) Regions in the autosomal DNA under positive selection



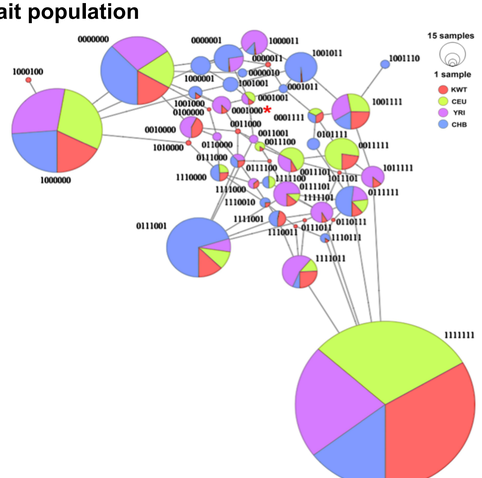
All the 385 SNPs under putative positive selection assigned to 100-kb windows. Each colored bar is a 25-Mb-segment in the chromosome representing at least one 100-kb window. Colors reflect the number of SNPs under positive selection.

(2) Putatively selected *TNKS* haplotype: chr8:9.3–9.7 Mb

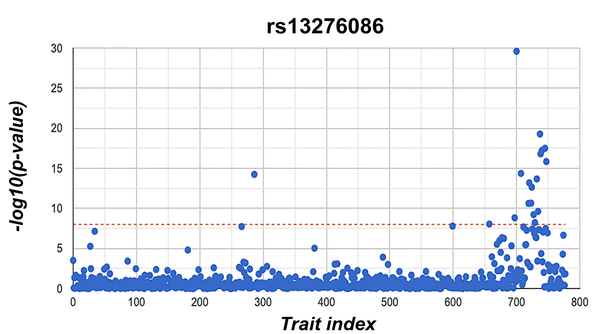


Selection scores for the selected seven SNPs are indicated by gray bars, their positions relative to *TNKS* are indicated by red small bars at the bottom.

(3) High frequency of the selected haplotype in the Kuwait population



(4) *TNKS* haplotype related to obesity, hypertension & asthma



GeneATLAS PheWAS results for one of the putatively. Selected SNPs, rs13276086. In total, 17 phenotypic traits revealed an association above the threshold (-log10[p-value] > 8, red dashed line).

DISCUSSION

(1) Adaptation to faster metabolism and fitness advantage in Kuwaiti ancestors

- Harsh desert climate of the Kuwait region could have driven this selection.
- *TNKS* haplotype exemplifies a general trend in which a more rapid metabolism rate and hypertension have been selected in the Kuwait population, which increased the allele frequency of multiple haplotypes.
- This likely conferred some degree of fitness advantage to ancestors of present-day Kuwaiti populations to survive in the extremely dry and hot ecological environments.

(2) Is this selection detrimental to the present-day Kuwaiti population?

- High prevalence of hypertension (25.3%) & obesity (48.2%), often attributed to drastic changes in the lifestyles and behaviors associated with westernization following oil discovery.
- Our results suggest that past adaptive trends have further predisposed Kuwaiti populations to the illnesses above at the genetic level.
- Overall, the mechanisms through which the *TNKS* haplotype conferred a fitness advantage and how the same haplotype predisposes the population to metabolic diseases remain fascinating areas that could be explored in future research.

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