## How climate change shaped evolution in the Middle East

Researchers at the University of Birmingham and the Wellcome Sanger Institute, along with their international collaborators, have uncovered signals in DNA that indicate a population boom in the Levant coinciding with the transition to agriculture and a population crash in Arabia as the region dried up.

Published in Cell, this is the first comprehensive population-scale study of Middle Eastern DNA. It used linked-read sequencing, a technique which enabled the team to reconstruct the population history of the region in unprecedented detail. As well as providing insights into ancient human history, these data will be an important resource for the study of genetic health and adaptations, such as type 2 diabetes and lactose tolerance, in Middle Eastern populations.

The fortunes of ancient human populations in the Middle East have been greatly influenced by its technological and climatic history. The area known as the Levant is regarded as a birthplace of agriculture, whereas the area known as Arabia is today dominated by the largest sand desert in the world [1].

Up until around 6,000 years ago, however, Arabia was a much wetter and greener place until the climate began to change and create the desert we see today. Another aridification event around 4,000 years ago, one of the most important climatic events in the last 10,000 years, resulted in an aridification phase of the region [2].

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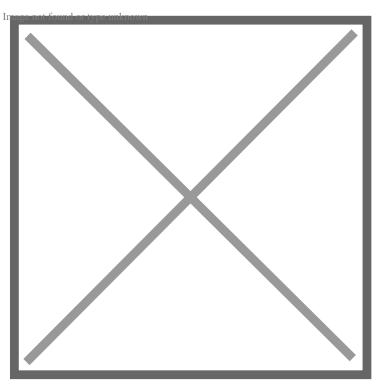
Until now, the Middle East has been understudied in genomic research. Because human diversity and the susceptibility to diseases vary between different populations, lack of detailed genetic data can exacerbate health inequalities.

In this study, researchers at the Wellcome Sanger Institute collected 137 samples from individuals representing eight Middle Eastern populations [3] and sequenced them using linked-read sequencing. The genomic data were then analysed at the Wellcome Sanger Institute and the University of Birmingham to look for variations in the genomes that could be used to map out human evolution from 100,000 years ago to the present day.

The team identified 23.1 million variations in the letters of DNA that comprise the human genome, known as single nucleotide variations (SNVs). Of these, 4.8 million SNVs were new variants not previously discovered in other populations. While many of these were rare, around 370,000 were common, and any of them could hold medical relevance.

This analysis revealed that human populations in the Levant experienced massive population growth in the last 15,000 years, which includes the time of the transition to agriculture. But populations in Arabia,

who had transitioned to a herder-gatherer lifestyle, experienced a population crash during the aridification of the region. Around 4,000 years ago, Levantine populations also suffered a crash as the region dried up. These population crashes resulted in evolutionary bottlenecks that constrained genetic diversity and still have medical relevance for Middle Eastern individuals today.



Dr. Mohamed Almarri. Credit: Wellcome Sanger Institute

<u>Dr Mohamed Almarri</u>, first author of the study from the Wellcome Sanger Institute, said: "Our study helps to uncover the hidden genetic diversity in the Middle East, which has been largely understudied until now. As well as identifying variants that provide fascinating insights into the lives and adaptation of Middle Eastern ancestors, some of these variants are also important for healthcare in the region today. For example, we detected variants that were beneficial in the past, but today increase the risk of type 2 diabetes in some Arabian groups."

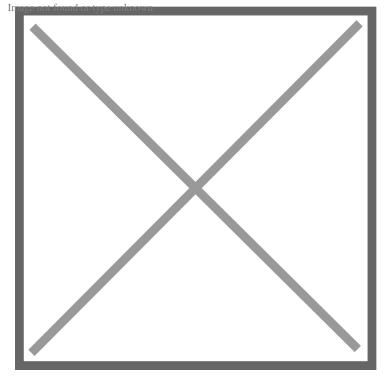
Clues to how Middle Eastern populations adapted to their changing circumstances can be found in their DNA. Those that helped humans adapt to their environment would have been under positive selection and increased in frequency.



Dr. Marc Haber. Credit: Wellcome Sanger Institute

<u>Dr Marc Haber</u>, corresponding author of the study from the University of Birmingham, said: "One interesting example of positive selection in our study was a variant associated with the ability to digest lactose in milk beyond childhood. In the last 8,000 years this variant increased to a frequency of 50 per cent in Arabians, coinciding with the transition from a hunter-gatherer to herder-gatherer lifestyle. This variant is much rarer in the Levant, and almost absent outside the region."

Looking even further back in time, the researchers also found that Arabian groups have the lowest Neanderthal ancestry of any known non-African population; instead much of their ancestry comes from an ancient 'ghost' population that likely did not interbreed with Neanderthals. This finding lends weight to a recent theory [4] about a mysterious 'ghost' population that may either have left Africa and stayed in the Middle East around 60,000 years ago, or remained in Africa until after the Neanderthals had disappeared.



Dr. Chris Tyler-Smith. Credit: Wellcome Sanger Institute

<u>Dr Chris Tyler-Smith</u>, senior author of the paper and an alumnus of the Wellcome Sanger Institute, said: "Linked-read sequencing provides the resolution that allows reconstruction of the genetic histories of human populations at a level of detail that was previously impossible. Such work provides fascinating stories about our ancient past, will help us to better understand genetic health and disease in Middle Eastern populations today, and brings us one step closer to recording the full richness of human diversity."

## Notes:

[1] The Levant refers to an area in the north of the Middle East, which includes modern-day Lebanon, Syria, Jordan, Israel and Palestine. South of this region is the Arabian Peninsula, an area dominated by the Arabian Desert, which includes Oman, Saudi Arabia, Yemen and the United Arab Emirates (UAE). [2] Known as the 4.2 kiloyear event, it was so severe that it has been suggested that it caused the collapse of multiple empires in the region, including the Old Kingdom in Egypt and the Akkadian Empire in Mesopotamia. [3] The term 'Arabian' in this study refers to samples from the Arabian Peninsula (Emirati, Saudi and Yemeni), Levantine for Syrians and Jordanians, and Iraqi-Arabs and Iraqi-Kurds for samples from Iraq. [4] Lazaridis et al. (2016) <u>Genomic insights into the origin of farming in the ancient Near East.</u> Nature.

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