

Genome research explains human migration, evolution

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Indigenous Arabs are direct descendants of humans who migrated out of Africa, before others continued on to colonize Europe and Asia, according to new research from Weill Cornell Medicine in New York City and Qatar. In addition to shedding light on humanity's evolution, the conclusion highlights the importance of taking population genetics into account when researching disease and developing treatments.

The investigation, published online Jan. 4 in *Genome Research*, sequenced the genomes of 104 Arabian Peninsula natives and compared them with 1,092 genomes from worldwide populations. The researchers compared each pair of genomes in the sample, which allowed them to cluster research participants by genome similarity so that an evolutionary tree emerged. The genomes of indigenous Arabs resulted in a unique cluster separate from the initial African population, illustrating the formation of a distinct population. European and Asian clusters diverged after the Arab population.

These genetic groupings help disentangle the ancient path of human evolution. Scientists previously hypothesized that when humans migrated out of Africa 125,000-60,000 years ago, they passed through the Arabian Peninsula, colonized Europe and Asia, and later returned. By contrast, the current findings demonstrate humans established the indigenous Arab population first.

"The indigenous Arab population was relatively isolated and yet they flourished and developed, as did Europeans, as did Asians. It's



fascinating that all of these populations arose separately, yet became equally sophisticated and impressively advanced," said lead author Jason Mezey, an associate professor of genetic medicine at Weill Cornell Medicine and of biological statistics/computational biology at Cornell University.

Identifying these distinct populations highlights how different groups can have subtle genetic differences – differences that demonstrate the importance of medical research being conducted based on specific populations. Diabetes, for example, affects about 22 percent of the Qatari population. The scientists say that basing diabetes research and treatment development on Qataris' precise genetic makeup – rather than on another population – will ensure optimal health results.

"When you're researching genetics to try to understand influences on human disease, you have to compare apples to apples, not oranges to apples," said senior author Dr. Ronald Crystal, chairman of the Department of Genetic Medicine, the Bruce Webster Professor of Internal Medicine, and a professor of genetic medicine and of medicine at Weill Cornell Medicine. "This is important for understanding the risk of disease in the Arab population – or any population – and using the correct population for the basis of comparison."

Advancements in genetic technology enabled the scientists to arrive at their findings, they said. Previous genome sequencing methods only allowed researchers to primarily investigate mitochondrial DNA, a limited portion of a cell's DNA inherited from one's mother, and the Y-chromosome, another small piece passed from father to son. These two components comprise a tiny fraction of the entire 3 billion base-pair genome. However, next-generation sequencing provides investigators with the opportunity to sequence a person's complete genome, compare it with others, and shed light on complex patterns of human evolution.



"Everyone wants to know where they're from," said lead author Juan Rodriguez-Flores, an instructor in genetic medicine at Weill Cornell Medicine. "Genetics is one way of learning about your ancestors. We have a technology that allows you to go back farther than anyone previously has."

More information: Juan L. Rodriguez-Flores et al. Indigenous Arabs are descendants of the earliest split from ancient Eurasian populations, *Genome Research* (2016). DOI: 10.1101/gr.191478.115

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