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Genetics agrees: Africa is thriving in diversity

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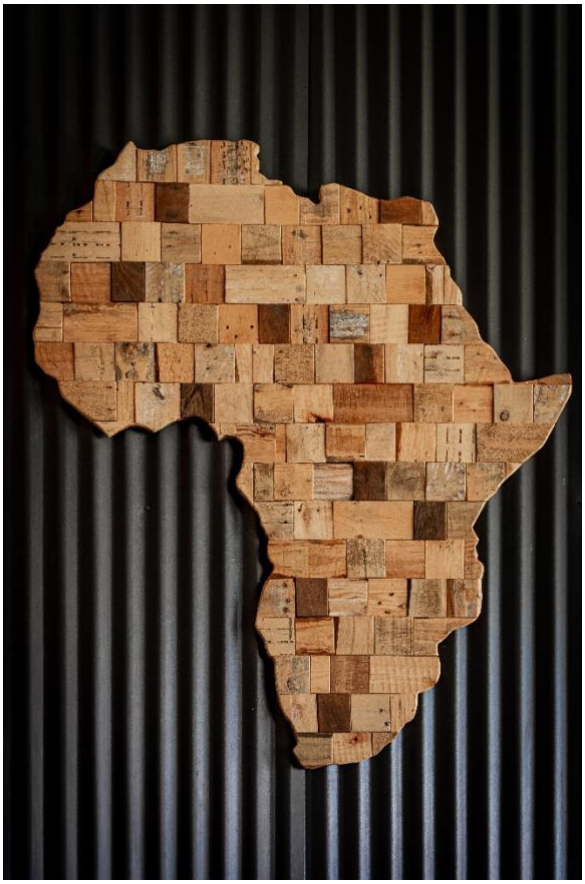
Populations in African countries have much more genetic variation than previously thought. We sequenced the DNA of 400 individuals and showed how people moved and interacted both with each other and with their environment in the past. Our findings, including both old and newly discovered gene variants, have deep implications for the future of genetics in medicine.



Since the Human Genome Project published the first sequence of the human DNA code in 2001, the field of human genetics has dramatically expanded. New studies have identified specific changes in the DNA code (or genetic variants) that are linked to why some people are more prone to get certain common diseases or to develop rare, one in a million, disorders. The vast majority of these studies were performed in persons identifying as (white) European Ancestry; most available genetic data come from just three countries – the UK (40%), the US (19%) and Iceland (12%). Other ancestral or ethnic groups, especially persons of African heritage, have been repeatedly left out. Individuals of African ancestry can contribute to significant advances in medicine through our DNA code. How? Africa is the home of modern mankind – most populations can trace their lineage back to Africa, with waves of migrations out of Africa serving to populate the wider world. In those migrations, however, only a small subgroup of the -more than- 2000 different ethnic language groups in Africa moved. As a result, in every study of DNA sequence changes at the population level, persons of African heritage have more variation per person (or per genome) than

any other continental group. This additional variation could hold the key to understanding diseases and health, not just in persons of African ancestry, but in anyone.

The Human Heredity and Health in Africa (H3Africa) project was conceived to fill the gap in diversity among human genetic studies that has continued to widen over the past two decades. Our study involved 426 individuals from 13 African countries, belonging to more than 50 different ethnolinguistic groups; one of the most diverse African groups ever to be included in such an investigation. The DNA of each participant underwent a procedure called whole genome sequencing. In simple terms, each of the 3 million DNA bases comprising the human genome was screened to look for variations from the current reference genome.

First, we counted the number of variants that were not seen in publicly available databases of sequence variation. Surprisingly, from only 400 individuals we identified more than 3 million variants that had not been seen or described previously. Most of these variants belonged to the ethnic language groups that had not been sequenced before and could be linked to diseases in the future. Among the variants that were not new, several were identified as "very rare" in the existing databases. Some of those existing variants had even been suggested to be causing rare diseases, largely because they were so rare; yet many of these same variants were very common in one or more of our populations. Our interpretation was that these variants aren't really causing disease, since they are too common for how rare the diseases are. These will need to be re-classified. For patients with rare diseases, it is important to identify the true cause of their disease; our resource of sequence information from African populations will help to do that better.

Next, we compared variations across our groups and inferred past historical interactions between them. In doing so, we were able to add details to one of the great migrations of Africa – known as the Bantu migration. As early men migrated from west to central Africa, they likely went through Zambia before turning further south and east. Interestingly, we found unexpected evidence of east African ancestry in one of the largest Nigerian (west African) ethnic language groups. Similarly, we also found several never-before described regions of DNA with evidence of natural selection, or else, evidence that the genetic variation in that region might be advantageous to the humans that carry them.

These examples of interactions between different groups, or with different environments or infectious agents, is part of what makes the African genome unique. It also makes it almost impossible to use DNA sequence information from a single country or group to represent all of Africa. Genetics is central to future attempts to provide 'precision medicine' - choosing the right healthcare model or medicine for the right individual at the right time. It is therefore essential to keep adding more genomic data from all global populations – including Africa – to ensure that everyone can benefit from the advances that genetics offers in health.