Ancient DNA reveals new branches of the Denisovan family tree

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A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

It's widely accepted that anatomically modern humans interbred with their close relatives, the Neanderthals and Denisovans, as they dispersed out of Africa. But a study examining DNA fragments passed down from these ancient hominins to modern people living in Island Southeast Asia and New Guinea now suggests that the ancestry of Papuans includes not just one but two distinct Denisovan lineages, which had been separated from each other for hundreds of thousands of years. In fact, the researchers suggest, one of those Denisovan lineages is so different from the other that they really should be considered as an entirely new archaic hominin species.

The findings, based on a new collection of genome data made possible by study co-authors from Eijkman Institute for Molecular Biology in Jakarta, Indonesia, appear April 11 in the journal *Cell*. Taken together with previous work—which has pointed to a third Denisovan lineage in the genomes of modern Siberians, Native Americans, and East Asians—the evidence "suggests that modern humans interbred with multiple Denisovan populations, which were geographically isolated from each other over deep evolutionary time," the researchers write.

The new findings show that modern humans making their way out of Africa for the first time were entering a new world that looked entirely different from the one we see today. "We used to think it was just us—modern humans—and Neanderthals," says senior author Murray Cox of Massey University in New Zealand. "We now know that there was a huge diversity of human-like groups found all over the planet. Our ancestors came into contact with them all the time."

The new evidence also unexpectedly shows extra mixing between Papuans and one of the two Denisovan groups, suggesting that this group actually lived in New Guinea or its adjacent islands. "People used to think that Denisovans lived on the Asian mainland and far to the north," says Cox. "Our work instead shows that the center of archaic diversity

was not in Europe or the frozen north, but instead in tropical Asia."

It had already been clear that Island Southeast Asia and New Guinea was a special place, with individuals there carrying more archaic hominin DNA than anywhere else on Earth. The region also was recognized as key to the early evolution of Homo sapiens outside Africa. But there were gaps in the story.

To help fill those gaps, Cox's team excavated archaic haplotypes from 161 new genomes spanning 14 island groups in Island Southeast Asia and New Guinea. Their analyses uncovered large stretches of DNA that didn't jibe with a single introgression of genes from Denisovans into humans in the region. Instead, they report, modern Papuans carry hundreds of gene variants from two deeply divergent Denisovan lineages. In fact, they estimate that those two groups of Denisovans had been separated from one another for 350,000 years.

The new findings highlight how "incredibly understudied" this part of the world has been, the researchers say. To put it in context, many of the study's participants live in Indonesia, a country the size of Europe that is the 4th largest country based on the size of its population. And yet, apart from a couple of genomes reported in a global survey of genomic diversity in 2016, the new paper reports the first Indonesian genome sequences. There also has been a strong bias in studies of archaic hominins to Europe and northern Eurasia because DNA collected from ancient bones survives best in the cold north.

This lack of global representation in both ancient and modern genome data is well noted, the researchers say. "However, we don't think that people have really grasped just how much of a bias this puts on scientific interpretations—such as, here, the geographical distribution of archaic hominin populations," Cox says.

As fascinating as these new findings are, the researchers say their primary aim is to use this new genomic data to help improve healthcare for people in Island Southeast Asia. They say this first genome survey in the region now offers the baseline information needed to set that work in motion.

More information: *Cell*, Jacobs et al.: "Multiple deeply divergent Denisovan ancestries in Papuans" www.cell.com/cell/fulltext/S0092-8674(19)30218-1 , DOI: 10.1016/j.cell.2019.02.035

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