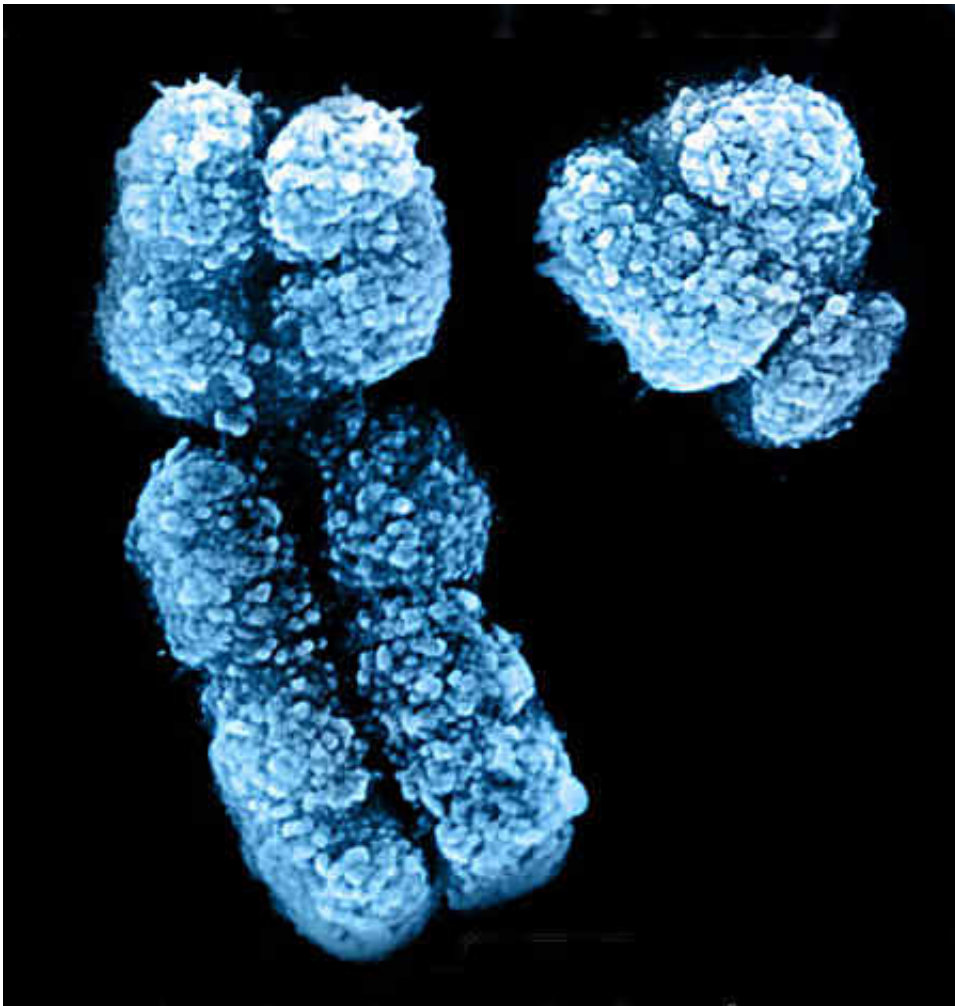


Modern men lack Y chromosome genes from Neanderthals, researchers say

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Although it's widely known that modern humans carry traces of

Neanderthal DNA, a new international study led by researchers at the Stanford University School of Medicine suggests that Neanderthal Y-chromosome genes disappeared from the human genome long ago.

The study will be published April 7 in *The American Journal of Human Genetics*, in English and in Spanish, and will be available to view for free. The senior author is Carlos Bustamante, PhD, professor of biomedical data science and of genetics at the School of Medicine, and the lead author is Fernando Mendez, PhD, a postdoctoral scholar at Stanford.

The Y chromosome is one of two human sex [chromosomes](#). Unlike the X chromosome, the Y chromosome is passed exclusively from father to son. This is the first study to examine a Neanderthal Y chromosome, Mendez said. Previous studies sequenced DNA from the fossils of Neanderthal women or from mitochondrial DNA, which is passed to children of either sex from their mother.

Other research has shown that the DNA of [modern humans](#) is from 2.5 to 4 percent Neanderthal DNA, a legacy of breeding between modern humans and Neanderthals 50,000 years ago. As a result, the team was excited to find that, unlike other kinds of DNA, the Neanderthal Y chromosome DNA was apparently not passed to modern humans during this time.

"We've never observed the Neanderthal Y chromosome DNA in any human sample ever tested," Bustamante said. "That doesn't prove it's totally extinct, but it likely is."

Why no Neanderthal DNA?

Why is not yet clear. The Neanderthal Y chromosome genes could have simply drifted out of the human gene pool by chance over the millennia.

Another possibility, said Mendez, is that Neanderthal Y chromosomes include genes that are incompatible with other [human genes](#), and he and his colleagues have found evidence supporting this idea. Indeed, one of the Y chromosome genes that differ in Neanderthals has previously been implicated in transplant rejection when males donate organs to women.

"The functional nature of the mutations we found," said Bustamante, "suggests to us that Neanderthal Y chromosome sequences may have played a role in barriers to gene flow, but we need to do experiments to demonstrate this and are working to plan these now."

Several Neanderthal Y chromosome genes that differ from those in humans function as part of the immune system. Three are "minor histocompatibility antigens," or H-Y genes, which resemble the HLA antigens that transplant surgeons check to make sure that organ donors and organ recipients have similar immune profiles. Because these Neanderthal antigen genes are on the Y chromosome, they are specific to males.

Theoretically, said Mendez, a woman's immune system might attack a male fetus carrying Neanderthal H-Y genes. If women consistently miscarried male babies carrying Neanderthal Y chromosomes, that would explain its absence in modern humans. So far this is just a hypothesis, but the immune systems of modern women are known to sometimes react to male offspring when there's genetic incompatibility.

When did we part ways?

The Y chromosome data also shed new light on the timeline for the divergence of humans and Neanderthals. The human lineage diverged from other apes over several million years, ending as late as 4 million years ago. After the final split from other apes, the human lineage branched into a series of different types of humans, including separate

lineages for Neanderthals and what are now modern humans.

Previous estimates based on mitochondrial DNA put the divergence of the human and Neanderthal lineages at between 400,000 and 800,000 years ago. The last common ancestor of Neanderthals and humans—based on the Y chromosome DNA sequenced in the study—is about 550,000 years ago.

Sequencing the Neanderthal Y chromosome may shed further light on the relationship between humans and Neanderthals. One challenge for the research team is to find out whether the Y chromosome Neanderthal gene variants identified were indeed incompatible with human genes.

The data for the study came from public gene sequencing databases. "We did not collect any data for this work," said Mendez. "It was all public data."

More information: *American Journal of Human Genetics*, Mendez et al.: "The divergence of Neanderthal and modern human Y chromosomes" [dx.doi.org/10.1016/j.ajhg.2016.02.023](https://doi.org/10.1016/j.ajhg.2016.02.023)

Provided by Stanford University Medical Center

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