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SCIENCE

A New Theory on How Neanderthal DNA Spread in Asia

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In 2010, scientists made a startling discovery about our past: About 50,000 years ago, Neanderthals interbred with the ancestors of living Europeans and Asians.

Now two teams of researchers have come to another intriguing conclusion: Neanderthals interbred with the ancestors of Asians at a second point in history, giving them an extra infusion of Neanderthal DNA.

The findings are further evidence that our genomes contain secrets about our evolution that we might have missed by looking at fossils alone. “We’re learning new, big-picture things from the genetic data, rather than just filling in details,” said Kirk E. Lohmueller, a geneticist at the University of California, Los Angeles, and co-author of one of the new studies.

The oldest fossils of Neanderthals date back about 200,000 years, while the most recent are an estimated 40,000 years old. Researchers have found Neanderthal bones at sites across Europe and western Asia, from Spain to Siberia.

Some of those bones still retain fragments of Neanderthal DNA. Scientists have pieced those DNA fragments together, reconstructing the entire Neanderthal genome. It turns out that Neanderthals had a number of distinct genetic mutations that living humans lack. Based on these differences, scientists estimate that the Neanderthals’ ancestors diverged from ours 600,000 years ago.

Our own ancestors remained in Africa until about 60,000 years ago, then expanded across the rest of the Old World. Along the way, they encountered Neanderthals. And our DNA reveals that those encounters led to children.

Today, people who are not of African descent have stretches of genetic material almost identical to Neanderthal DNA, comprising about 2 percent of

their entire genomes. These DNA fragments are the evidence that Neanderthals interbred with the early migrants out of Africa, likely in western Asia.

Researchers also have found a peculiar pattern in non-Africans: People in China, Japan and other East Asian countries have about 20 percent more Neanderthal DNA than do Europeans.

Last year, Sriram Sankararaman, a postdoctoral researcher at Harvard Medical School, and his colleagues proposed that natural selection was responsible for the difference. Most Neanderthal genes probably had modestly bad effects on the health of our ancestors, Dr. Sankararaman and other researchers have found. People who inherited a Neanderthal version of any given gene would have had fewer children on average than people with the human version.

As a result, Neanderthal DNA became progressively rarer in living humans. Dr. Sankararaman and his colleagues proposed that it disappeared faster in Europeans than in Asians. The early Asian population was small, the researchers suggested, and natural selection eliminates harmful genes more slowly in small groups than in large populations. Today, smaller ethnic groups, like Ashkenazi Jews and the Amish, can have unusually high rates of certain genetic disorders.

Joshua M. Akey, a geneticist at the University of Washington, and the graduate student Benjamin Vernot recently set out to test this hypothesis. They took advantage of the fact that only some parts of our genome have a strong influence on health. Other parts — so-called neutral regions — are less important.

A mutation in a neutral region won't affect our odds of having children and therefore won't be eliminated by natural selection. If Dr. Sankararaman's hypothesis were correct, you would expect Europeans to have lost more harmful Neanderthal DNA than neutral DNA. In fact, the scientists did not find this difference in the DNA of living Europeans.

Dr. Akey and Mr. Vernot then tested out other possible explanations for the comparative abundance of Neanderthal DNA in Asians. The theory that made the most sense was that Asians inherited additional Neanderthal DNA at a later time.

In this scenario, the ancestors of Asians and Europeans split, the early Asians migrated east, and there they had a second encounter with Neanderthals. Dr. Akey and Mr. Vernot reported their findings in the American Journal of Human Genetics.

Dr. Lohmueller and the graduate student Bernard Y. Kim approached the same genetic question, but from a different direction. They constructed a

computer model of Europeans and Asians, simulating their reproduction and evolution over time. They added some Neanderthal DNA to the ancestral population and then watched as Europeans and Asian populations diverged genetically.

The scientists ran the model many times over, trying out a range of likely conditions. But no matter which variation they tried, they couldn't find one explaining why Asians today have extra Neanderthal DNA.

But when they ran a model that included a second interbreeding, another "pulse" of Neanderthal genes into the Asian population, the researchers had better luck. "We find that the two-pulse model can fit the data really well," Dr. Lohmueller said. He and Mr. Kim published their results in a separate paper in the American Journal of Human Genetics.

Dr. Akey is pleased that the two studies reached the same conclusion. "Together, they tell the same story, just from different perspectives," he said.

Dr. Sankararaman agreed that the new research cast doubt on his proposal that natural selection stripped Neanderthal DNA from Europeans more quickly than from Asians. "The analysis from both papers gives strong support to the two-pulse model in Asians," he said.

But the two-pulse hypothesis also poses a puzzle of its own.

If Neanderthals became extinct 40,000 years ago, they may have disappeared before Europeans and Asian populations genetically diverged. How could there have been Neanderthals left to interbreed with Asians a second time?

It is conceivable that the extinction of the Neanderthals happened later in Asia. If that is true, there might yet be more recent Neanderthal fossils waiting to be discovered there.

Or perhaps Asians interbred with some other group of humans that had interbred with Neanderthals and carried much of their DNA. Later, that group disappeared.

"That's a paradox the field needs to address," Dr. Lohmueller said.
