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An ancient affair: a Neandertal woman and a Denisovan man had a daughter

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ABSTRACT

We sequenced the genome of a ~90,000-year-old individual and discovered that she had a Neandertal mother and a Denisovan father. This shows that people from different prehistoric hominin groups occasionally met, interacted, and had

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In prehistoric times, at least two groups of hominins (that is, the entity which includes humans and their closest relatives) inhabited Eurasia: Neandertals, who lived throughout Europe and the Near East, and Denisovans, who likely lived in Asia. Genetically, Neandertals and Denisovans were more different from each other than any two people living today. Both groups were distantly related to early humans, our own ancestors. Denisova Cave, an archaeological site in southern Siberia, is so far the only place in the world where researchers have found remains of both Neandertals and Denisovans - making it a fascinating place to study these ancient hominins.

Geneticists can infer how closely or distantly related two individuals are by comparing sequence variants in their genomes, the complete sets of their DNA. DNA is a molecule that encodes the list of instructions necessary to build an organism. Since it is passed through from generation to generation, our DNA contains information about the history of our ancestors. In Denisova Cave, DNA tends to preserve well over very long periods of time. Researchers have already succeeded in reconstructing the complete genomes of a ~120,000-year-old Neandertal and a ~70,000-year-old Denisovan from bones excavated at the site.

One of the challenges of ancient DNA research is that remains of ancient hominins are hard to come by. Archaeologists excavate thousands of bone fragments each year at Denisova Cave, but even experts can identify only about 5% of them based on their shape and structure. To overcome this problem, scientists can now analyze the proteins in ancient bones to tell apart human and animal remains. We applied this method to around 2,000 bone fragments from the site. We identified one,

"Denisova 11", to be a part of a hominin skeleton. Based on its size, it was likely a part of an arm or a leg bone of someone who was at least 13 years old. We sequenced and analyzed the genome of this individual - first to determine whether the bone came from a Neanderthal or a Denisovan; and second, to find clues about the ancient population this individual came from.

To answer our first question, we checked whether the DNA of Denisova 11 carried mostly Neandertal-like or mostly Denisovan-like sequence variants. To our surprise, we found that the genome contained both types of variants in almost equal proportions, indicating that Denisova 11 had both ancestries. This could mean either that Denisova 11's parents lived in a mixed population, or that one parent was a Neandertal and the other a Denisovan. To tell these two possible scenarios apart, we compared how the variants distributed throughout the genome in our observations versus what would be expected under each scenario. We found that the scenario in which each parent originated from a different group fitted the data best. We then added two more pieces of information to reconstruct Denisova 11's "family tree". First, that she was a female; second, that her mitochondrial DNA - the small part of the genome that only mothers pass on to their offspring - was of the Neandertal type. We concluded that Denisova 11 was the daughter of a Neandertal mother and a Denisovan father.

To address our second aim, we used Denisova 11's mixed ancestry to investigate both sides of her family, who lived around 90,000 years ago. Her mother was more closely related to a Neandertal that lived around 55,000 years ago in Croatia than to the roughly 120,000-year-old Neandertal from Denisova Cave. This indicates that Neandertals migrated between eastern and western Eurasia at least at one point in their history. We also discovered that her Denisovan father had small traces of Neandertal DNA in his genome. We inferred that these came from at least one Neandertal ancestor that lived some 10,000 to 15,000 years before him.

Studying the genome of Denisova 11, we found evidence for multiple instances of mixing between Neandertals and Denisovans: once between her parents, and at least once in the family history of her father. And yet, such events had to be rare, otherwise we would not be able to distinguish the two groups genetically. It is likely that the two groups overlapped little in space and in time, so that most individuals never had the opportunity to interact with someone from the other group. But when they did meet, the two groups clearly mixed. We also know about instances of Neandertals and Denisovans mixing with ancient humans. This means that throughout history, different groups of humans have always mixed.