Most-complete bonobo genome can reveal what makes us ‘uniquely human’

By Zack Fishman
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The bonobo Muhdeblu, pictured here with her newly born offspring in 2014, had her DNA sequenced in a recent genome study. (Claudia Philipp/Wuppertal Zoo)

A large collaboration of scientists has sequenced and identified more than 98% of the genes in a bonobo, one of humans' closest evolutionary cousins, revealing surprising speed and complexity in the evolution of genes within the great-ape family and marking a significant improvement from earlier sequencing.

The bonobo is the last of the great apes to have its DNA sequenced with modern technology, and the new genome sets the stage for future research into the lineage of humanity and its close relatives. The study was published Wednesday in *Nature*.

"A lot of changes have happened in terms of the evolution of man, and we believe those are encoded in our genomes," said Evan Eichler, a professor of genome sciences at the University of Washington and a senior author of the paper. "If you're going to characterize those types of mutation events that make us uniquely human, you have to have high-quality genomes of our closest related species — it's just that simple."

Native to Central Africa, bonobos are one of the eight species of great apes, a taxonomic family that also includes humans, chimpanzees, gorillas and orangutans. Bonobos and the closely related chimpanzees are the species most genetically similar to humans, with both sharing between about 98% and 99% of the same DNA with Homo sapiens.

The first bonobo genome was sequenced in 2012, and although it was very good given the technology available, according to Eichler, it was "Swiss cheese," with more than 108,000 gaps in the genetic code.

For the new genome, nearly 40 scientists sequenced the DNA of a female bonobo named Mudheblu, pronounced "moody blue," in Germany's Wuppertal Zoo. She was reported as being one of the few apes to show kindness to bullied British bonobo Bili, a zoo transfer whose abuse from other bonobos led to petitions for his removal. ("I have a morally aware bonobo that was sequenced!" Eichler said.)

In an effort beginning four years ago that Eichler described as a collective labor of love, the study's authors completely annotated more than 98% of the genes in the bonobo genome and closed more than 99% of the preexisting gaps. The project took advantage of long-read sequencing, a relatively new approach to sequencing DNA that processes long strings of base pairs at a time and has been used to obtain genomes of all other great apes.

The researchers compared the bonobo genome with those of humans and other great apes and found surprisingly rapid and complex genetic evolution. The team identified numerous genes that, between bonobos and chimpanzees, were possessed by only one of the species. The primates diverged into different species about 1.7 million years ago and only differ in DNA by about 0.4%, so these genetic differences must have arisen "in almost real time evolutionarily," according to Eichler, and knowing the now-identified genes could possibly be useful in understanding the animals' modern behavioral differences.

The analysis also found many parts of the genome in which humans are more similar to either bonobos or chimpanzees than the non-human primates are to each other — this is the case for 5.1% of the human genome, higher than the 3.3% found by the previous bonobo genome.

The phenomenon, called incomplete lineage sorting, is unusual because humans diverged from the bonobo-chimp evolutionary line between about 7 million and 13 million years ago, long before the bonobo and chimpanzee split into different species. But through a proc[illegible]ineage sorting, a species may not share a gene or variant with a

close relative while sharing it with a more distant relative.

Furthermore, about one-quarter of the genes found to be subject to incomplete lineage sorting were not randomly distributed, a new finding that breaks from the usual understanding on how the phenomenon occurs. Some of them were associated with immune response or cell growth, and this non-random group may suggest that they hold a past or present evolutionary benefit, Eichler said.

"We have something really new, compared to the other genome," said Mario Ventura, another senior author of the paper and an associate professor of biology at the University of Bari Aldo Moro. "We're interested to understand what's the effect on gene[s], gene function and stuff like that."

With the Mudheblu genome openly available to scientists, there is still more work to be done on the bonobo genome, according to Eichler. Sequencing the genomes of other bonobos would allow for investigations into variance within the species, he said.

The professor also wants to close the fewer than 1,000 gaps remaining and finish the genome. Many of the gaps are of dynamic genes and may contain important genetic information, he said, much like how some of the last gene gaps filled in the human genome were connected to larger brains and greater interconnectivity between individuals.

Such research could inform conservation efforts for bonobos, which are endangered and hunted for meat in the Democratic Republic of the Congo, their sole habitat.

"I firmly believe that there is more there to be discovered, more genetic differences that are really dynamic that have really radically changed gene content and structure between us and other species," Eichler said, "and they're precisely in these areas that have not been picked up."a

The study, "A high-quality bonobo genome refines the analysis of hominid evolution," published May 5 in Nature, was authored by Yafei Mao, LaDeana Hillier, David Porubsky, Ruiyang Li, Arvis Sulovari, David Gordon, Shwetha Murali, Philip Dishuck, PingHsun Hsieh, William Harvey, Peter Audano, Katherine Munson, Alexandra Lewis, Carl Baker, Kendra Hoekzema, Tzu-Hsueh Huang, Melanie Sorensen and Evan Eichler, University of Washington; Claudia Catacchio, Ludovica Mercuri, Ilaria Piccolo, Francesca Antonacci and Mario Ventura, University of Bari Aldo Moro; Jason Fernandes, Marina Haukness, Ian Fiddes, Sofie Salama, Benedict Paten and Mark Diekhans, University of California, Santa Cruz; Francesco Montinaro, University of Bari Aldo Moro and Institute of Genomics, University of Tartu; Jessica Storer, Institute for Systems Biology; Jason Underwood, Pacific Biosciences of California; Jerilyn Walker and Mark Batzer, Louisiana State University; Jinna Hoffman and Françoise Thibaud-Nissen, National Institutes of Health; and Andy Pang, Joyce Lee a[illegible] o Genomics.