

Last Update 28 April 2023, To learn more about humans, a large international team of scientists spent years tracking down some of the strangest creatures on Earth. They camped out on an Arctic ice floe to collect DNA from the one-tusked narwhal, netted a tiny bumblebee bat in a cave-rich region of Southeast Asia and ventured behind the scenes at a Caribbean zoo to draw blood from the slender-snouted solenodon, one of the world's few venomous mammals. Researchers compared the genomes of these mammals with those of a diverse assortment of others, including an armadillo, a meerkat, a star-nosed mole and a human. In doing so, they were able to identify stretches of DNA that have barely changed over eons of mammalian evolution and are thus likely to be vital to human health and functioning. The genetic database they assembled includes the complete genomes of 240 species, covering more than 80 percent of the planet's mammalian families (and including humans). It could help scientists answer a wide variety of questions about other animals, such as when and how they evolved and the biological basis for some of their unusual talents. "What amazingly cool things can those species do that humans can't do?" said Elinor Karlsson, a geneticist at UMass Chan Medical School and the Broad Institute and a co-leader of what is known as the Zoonomia Project. "We always like to think of humans as being the most special species. But it turns out that we're really quite boring in many ways." A narwhal captured to collect genetic samples and to study its tusk. Gretchen Freund The Zoonomia data set has limitations. It contains just one genome per species (with the exception of the domestic dog, which was sequenced twice), and thousands of mammals are missing. But in a new package of papers, published in Science on Thursday, the Zoonomia team showcased the power of this kind of multispecies data. And it's just the beginning. "Sequencing a lot of genomes is not trivial," said Michael G. Campana, a computational genomics scientist at the Smithsonian's National Zoo and Conservation Biology Institute, who was not part of the project. "What's really important is actually making use of these data." Here are some of the things that Zoonomia scientists are already doing with it: Uncovering the basis of special skills To look for the underpinnings of exceptional animal talents, the scientists sought genetic sequences that had evolved unusually quickly in species that shared a certain trait, such as the ability to hibernate. In one analysis, the researchers focused on deep hibernators, such as the fat-tailed dwarf lemur and the greater mouse-eared bat, which can maintain low body temperatures for days or weeks at a time. The researchers found evidence of "accelerated evolution" in a variety of genes, including one that is known to help protect cells from temperature-related stress and another that inhibits a cellular pathway related to aging. "Lots of hibernating species also have exceptional longevity," Dr. Karlsson said, leading her to wonder: Do the changes in that gene contribute to their long lives? The researchers also explored the mammalian sense of smell. Animals have a large assortment of different olfactory receptors, each capable of binding to certain odor-causing molecules; species with more olfactory receptor genes generally have keener senses of smell. A Hoffmann's two-toed sloth, which has nearly as many olfactory receptor genes as the nine-banded armadillo. Milan Zymunt/Alamy When the Zoonomia team tallied the number of these genes in each species, the African savanna elephant took the top spot, with 4,199. The nine-banded armadillo and Hoffmann's two-toed sloth followed, while the Central American agouti came in fourth. The agouti "turns out to have one of the best olfactory repertoires of any mammal, for totally unknown reasons," Dr. Karlsson said. "It's a reminder of how much diversity there is out there that we don't know anything about." (Dogs, she noted, did not prove to be "particularly special" in this regard.) On the other hand, cetaceans — a group that includes dolphins and whales — have a notably small number of olfactory receptor genes, which makes sense given their watery habitats. "They communicate in other ways," said Kerstin Lindblad-Toh, a geneticist at the Broad Institute and Uppsala University and the other leader of the Zoonomia Project. Species with more olfactory receptor genes also tended to have more olfactory turbinates, bony structures in the nasal cavity that aid olfaction. The results suggest that "if certain traits are important, they evolve in multiple ways," Dr. Lindblad-Toh said. She added, "I think that one of the important things with our data set is that it generates the genome sequencing for so many different species that people can start looking at their favorite characteristics." Painting portraits of populations Balto, the Alaskan sled dog, in 1920. via The New York Times Photo Archives In February 1925, in the midst of a diphtheria outbreak, a relay of sled dog teams delivered an emergency supply of antitoxin to Nome, Alaska, which had been isolated by snow. Balto, one of the dogs that ran the final leg of the relay, became famous; when he died some years later, his taxidermied body was put on display at the Cleveland Museum of Natural History. A team of Zoonomia researchers has now used a small piece of that taxidermied tissue to learn more about the celebrity sled dog and his canine contemporaries. "We saw this as a little challenge," said Kathleen Morrill, an author of the Balto paper, who performed the research as a

graduate student at UMass Chan Medical School and is now a senior scientist at Colossal Biosciences. “Here is this one individual, really famed. We don’t know a lot about his biology. What can we say about his genome?” Balto, they found, was genetically “healthier” than modern purebred dogs, with more inherited genetic variation and fewer potentially harmful mutations. That finding likely stems from the fact that sled dogs are typically bred for physical performance and may be a mixture of breeds. Balto also had an assortment of genetic variants that were not present in wolves and were rare or missing in modern purebred dogs, the researchers found. Many variants were in genes involved in tissue development and may have affected a variety of traits important for sled dogs, such as skin thickness and joint formation. Balto had two copies of these variants, one inherited from each parent, which means they were probably at least somewhat common in other Alaskan sled dogs at the time. “We get this much clearer picture of what he was like and what his population would have looked like,” said Katie Moon, a postdoctoral researcher at the University of California, Santa Cruz, and an author of the paper. “And that picture is of really well-adapted working sled dogs.”

Illuminating evolutionary timelines An artist’s concept of Early Cretaceous mammals, including *Durlstodon ensomi*, upper left, and *Durlstotherium newmani*, foreground. At center, a dinosaur of the genus *Nuthetes* with a baby *D. newmani* in its beak. Mark P. Witton/Science Source

Scientists have long debated precisely how and when today’s diverse assortment of mammals came into being. Did the mammalian family tree branch out only after the extinction of the dinosaurs, some 66 million years ago? Or did the process largely take place before the catastrophe? A new analysis with the Zoonomia genomes suggests that the answer is both. Mammals first began to diversify about 102 million years ago, when Earth’s continents were fragmenting and sea levels began rising. “This isolated the predecessors of the modern lineages on different land masses,” said William Murphy, an evolutionary geneticist at Texas A&M University and an author of the paper. But another burst of diversification came after the extinction of the dinosaurs, the researchers found, when the emergence of new land and the disappearance of the reigning reptiles provided mammals with new habitats, resources and opportunities. “It’s a really landmark paper,” said Scott Edwards, an evolutionary biologist at Harvard, who was not involved in the research. “It’s probably the largest of its kind in terms of trying to put mammals on a time scale.” The Zoonomia package more broadly is “a monumental set of work,” he added. “It’s going to really set the standard for our understanding of mammal evolution going forward.”

Predicting extinction risk A Java mouse-deer fawn and its mother. Jorge Guerrero/Agence France-Presse — Getty Images

Mammals generally inherit two copies of most genetic sequences, one from each parent. Determining how closely these sequences match can provide insight into the size of past animal populations; long stretches of matching DNA can be a sign of inbreeding, for instance. The genome of a single animal reflects “how closely related its parents were, grandparents were, going all the way back,” said Aryn Wilder, a conservation geneticist at the San Diego Zoo Wildlife Alliance. Dr. Wilder and her colleagues used the Zoonomia genomes to estimate the population sizes of different species throughout history. Compared with species that were historically abundant, those with small past populations had more potentially harmful genetic mutations and were more likely to be classified as threatened by the International Union for Conservation of Nature. The researchers also analyzed the genomes of three species whose risk of extinction the I.U.C.N. considered to be unknown because of a lack of data: the killer whale, the Upper Galilee Mountains blind mole rat and the Java mouse-deer (which looks exactly as advertised). The results suggested that the killer whale might be at highest risk. The approach could provide a quick way to prioritize species for more thorough, resource-intensive risk assessments, said Beth Shapiro, a paleogeneticist at the University of California, Santa Cruz, and an author of the study. “It could be a relatively straightforward way to do conservation triage,” she said.

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