Feline genetics help pinpoint first-ever domestication of cats

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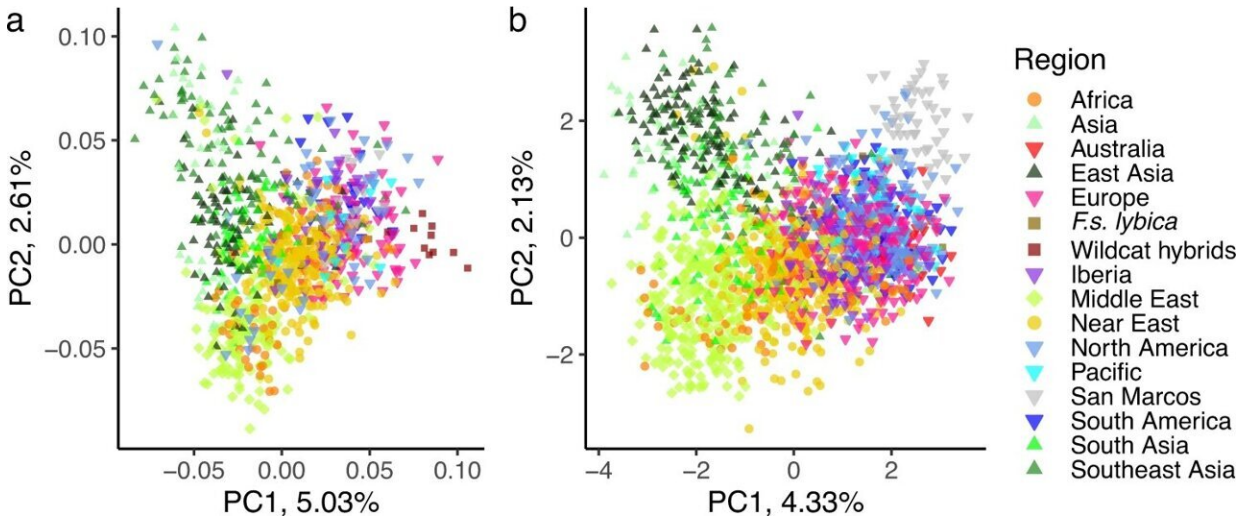

Principal component analyses (PCA) of genetic variation in random-bred and wildcat felines. **a** PCA plot of SNP data ($N = 983$). **b** PCA plot of STR data ($N = 1861$). A single point represents an individual, the shape represents a geographic region, the color represents a geographic sub-region. The two wildcat populations are denoted by squares of different colors. Middle Eastern, South Asia, and Western European cats form the peripheral subpopulations of random-bred cats. The wildcat hybrids and the island population of San Marcos, Baja California, are additional peripheral populations for **a** and **b**, respectively. Credit: *Heredity* (2022). DOI: 10.1038/s41437-022-00568-4

Nearly 10,000 years ago, humans settling in the Fertile Crescent, the areas of the Middle East surrounding the Tigris and Euphrates rivers,

made the first switch from hunter-gatherers to farmers. They developed close bonds with the rodent-eating cats that conveniently served as ancient pest-control in society's first civilizations.

A new study at the University of Missouri found this lifestyle transition for humans was the catalyst that sparked the world's first domestication of cats, and as humans began to travel the world, they brought their new feline friends along with them.

Leslie A. Lyons, a feline geneticist and Gilbreath-McLorn endowed professor of comparative medicine in the MU College of Veterinary Medicine, collected and analyzed DNA from cats in and around the Fertile Crescent area, as well as throughout Europe, Asia and Africa, comparing nearly 200 different genetic markers.

"One of the DNA main markers we studied were microsatellites, which mutate very quickly and give us clues about recent cat populations and breed developments over the past few hundred years," Lyons said.

"Another key DNA marker we examined were single nucleotide polymorphisms, which are single-based changes all throughout the genome that give us clues about their ancient history several thousands of years ago. By studying and comparing both markers, we can start to piece together the evolutionary story of cats."

Lyons added that while horses and cattle have seen various domestication events caused by humans in different parts of the world at various times, her analysis of feline genetics in the study strongly supports the theory that cats were likely first domesticated only in the Fertile Crescent before migrating with humans all over the world. After feline genes are passed down to kittens throughout generations, the genetic makeup of cats in western Europe, for example, is now far different from cats in southeast Asia, a process known as 'isolation by

distance.'

"We can actually refer to cats as semi-domesticated, because if we turned them loose into the wild, they would likely still hunt vermin and be able to survive and mate on their own due to their natural behaviors," Lyons said. "Unlike dogs and other domesticated animals, we haven't really changed the behaviors of cats that much during the domestication process, so cats once again prove to be a special animal."

Lyons, who has researched feline genetics for more than 30 years, said studies like this also support her broader research goal of using cats as a biomedical model to study genetic diseases that impact both cats and people, such as polycystic kidney disease, blindness and dwarfism.

"Comparative genetics and precision medicine play key roles in the 'One Health' concept, which means anything we can do to study the causes of genetic diseases in cats or how to treat their ailments can be useful for one day treating humans with the same diseases," Lyons said.

"I am building genetic tools, genetic resources that ultimately help improve cat health. When building these tools, it is important to get a representative sample and understand the genetic diversity of cats worldwide so that our genetic toolbox can be useful to help cats all over the globe, not just in one specific region."

Throughout her career, Lyons has worked with cat breeders and research collaborators to develop comprehensive feline DNA databases that the scientific community can benefit from, including cat genome sequencing from felines all around the world. In a 2021 study published in *Trends in Genetics*, Lyons and colleagues found that the cat's genomic structure is more similar to humans than nearly any other non-primate mammal.

"Our efforts have helped stop the migration and passing-down of

inherited genetic diseases around the world, and one example is polycystic kidney disease, as 38% of Persian cats had this disease when we first launched our genetic test for it back in 2004," Lyons said. "Now that percentage has gone down significantly thanks to our efforts, and our overall goal is to eradicate genetic diseases from cats down the road."

Currently, the only viable treatment for polycystic kidney disease has unhealthy side effects, including liver failure. Lyons is currently working with researchers at the University of California at Santa Barbara to develop a diet-based treatment trial for those suffering from the disease.

"If those trials are successful, we might be able to have humans try it as a more natural, healthier alternative to taking a drug that may cause liver failure or other health issues," Lyons said. "Our efforts will continue to help, and it feels good to be a part of it."

The new research was recently published in *Heredity*.

More information: Sara M. Nilson et al, Genetics of randomly bred cats support the cradle of cat domestication being in the Near East, *Heredity* (2022). DOI: 10.1038/s41437-022-00568-4

Leslie A. Lyons, Cats—telomere to telomere and nose to tail, *Trends in Genetics* (2021). DOI: 10.1016/j.tig.2021.06.001

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