Dogs likely originated in the Middle East, new genetic data indicate

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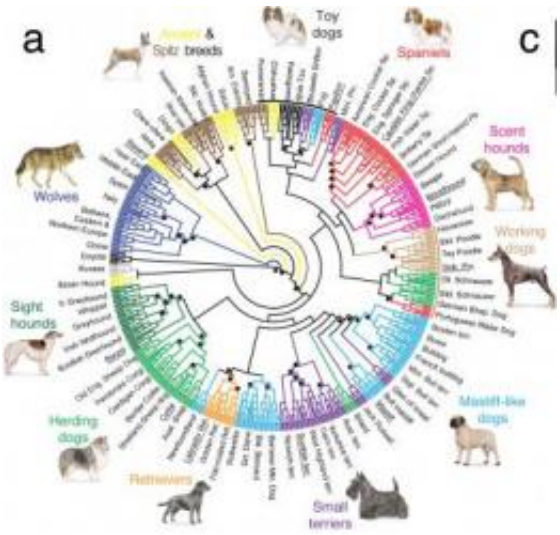

This evolutionary tree shows dog breeds and gray wolves. Credit: UCLA

Dogs likely originated in the Middle East, not Asia or Europe, according to a new genetic analysis by an international team of scientists led by UCLA biologists. The research, funded by the National Science Foundation and the Searle Scholars Program, appears March 17 in the advance online edition of the journal *Nature*.

"Dogs seem to share more genetic similarity with Middle Eastern gray wolves than with any other wolf population worldwide," said Robert Wayne, UCLA professor of ecology and evolutionary biology and senior author of the *Nature* paper. "Genome-wide analysis now directly

suggests a Middle East origin for modern dogs. We have found that a dominant proportion of modern dogs' ancestry derives from Middle Eastern wolves, and this finding is consistent with the hypothesis that dogs originated in the Middle East.

"This is the same area where domestic cats and many of our livestock originated and where agriculture first developed," Wayne noted.

Previous genetic research suggested an East Asian origin for dogs, "which was unexpected," Wayne said, "because there was never a hint in the archaeological record that dogs evolved there."

"We were able to study a broader sampling of wolves globally than has ever been done before, including Middle Eastern wolves," said the paper's lead author, Bridgett vonHoldt, a UCLA graduate student of ecology and evolutionary biology in Wayne's laboratory who studies the genetics of dog domestication. "In our analysis of the entire genome, we found that dogs share more unique markers with Middle Eastern wolves than with East Asian wolves. We used a genome-wide approach, which avoids the bias of single genome region."

The biologists report genetic data from more than 900 dogs from 85 breeds (including all the major ones) and more than 200 wild gray wolves (the ancestor of domestic dogs) worldwide, including populations from North America, Europe, the Middle East and East Asia. They used molecular genetic techniques to analyze more than 48,000 genetic markers. No previous study has ever analyzed anywhere near that many markers.

The biologists have samples from Israel, Saudi Arabia and Iran — but they have not pinpointed a specific location in the Middle East where dogs originated.

"This study is unique in using a particular technology called a single nucleotide polymorphism, or SNP, genotyping chip; these chips interrogate the nucleotides at 48,000 locations in the genome," said John Novembre, UCLA assistant professor of ecology and evolutionary biology and a member of UCLA's Interdepartmental Program in Bioinformatics. "We are able to compare dogs looking at not just one small part of the genome, but at 48,000 different locations. That gives us the fine-scale resolution to analyze how these breeds are related to one another and how they are related to wolves."

Previous genetic research had suggested an East Asian origin based on the higher diversity of mitochondrial sequences in East Asia and China than anywhere else in the world. (Mitochondria are tiny cellular structures outside the nucleus that produce energy and have their own small genome.) However, that research was based on only one sequence, a small part of the mitochondrial genome, Wayne noted.

"That research made extrapolations about how the domestic dog has evolved from examination of one region in the mitochondrial genome," Wayne said. "This new Nature paper is a much more comprehensive analysis because we have analyzed 48,000 markers distributed throughout the nuclear genome to try to conclude where the most likely ancestral population is.

"What we found is much more consistent with the archaeological record," he said. "We found strong kinship to Middle Eastern gray wolves and, to some extent, European gray wolves — but much less so to any wolves from East Asia. Our findings strongly contradict the conclusions based on earlier mitochondrial DNA sequence data."

Eighty percent of dog breeds are modern breeds that evolved in the last few hundred years, Wayne said. But some dog breeds have ancient histories that go back thousands of years.

"We sampled both groups, the modern explosion of dog breeds and some of the ancient lineages," he said. "Our data were aimed at resolving questions about the origin of domestic dogs, the evolution of dog breeds, and the history of dog breeds and relationships to their closest wild progenitor, the gray wolf."

The first dogs that appeared in the Middle Eastern archaeological record date back some 12,000 to 13,000 years, Wayne said. Wolves have been in the Old World for hundreds of thousands of years. The oldest dogs from the archaeological record come from Europe and Western Russia. A dog from Belgium dates back 31,000 years, and a group of dogs from Western Russia is approximately 15,000 years old, Wayne said.

"We know that dogs from the Middle East were closely associated with humans because they were found in ancient human burial sites," Wayne said. "In one case, a puppy is curled up in the arms of a buried human."

Some very old strains of dogs, with a history dating back more than several thousand years, may be mixed with modern breeds, enhancing their diversity in certain areas such as East Asia, Wayne said, interpreting the higher mitochondrial DNA diversity in that area of the globe.

There is one small set of East Asian breeds that does not indicate a strong Middle East origin, showing instead a high level of genetic sharing with Chinese wolves. This finding suggests there was some intermixing between East Asian dog breeds and East Asian wolves; the data do not make clear how long ago this occurred.

"However, the vast majority of dogs that we studied show significant levels of sharing with Middle Eastern wolves," said Novembre, a population geneticist who studies genetic diversity and the lessons that can be learned from it.

Co-authors on the *Nature* paper include a group of researchers from the National Institutes of Health/National Human Genome Research Institute led by Elaine Ostrander; a group led by Carlos Bustamante, formerly of the Cornell University Department of Biological Statistics and Computational Biology and now a professor of genetics at the Stanford University School of Medicine; and scientists from China, Israel, Australia, Europe and Canada.

"By analyzing a sea of scientific data, Bob Wayne and John Novembre are at the forefront of the 'new life sciences' — which represents new ways to make discovery," said Victoria Sork, dean of the UCLA Division of Life Sciences. "Their integration of genomic data with bioinformatic approaches illustrates how integration has enhanced our ability to analyze biological systems. Integration of knowledge is changing how we think about how life works. We are no longer limited to studying just one piece of a puzzle."

Toy dogs and an evolutionary framework for dog domestication

The biologists have also found that when one looks at a relationship tree of modern and ancient dog breeds, there is surprising structure to it, and the structure mimics the classifications of dogs by breeders into herding dogs, retrievers, sight hounds, small terriers and others.

"We found there is a surprising genetic structure that accords with functional classifications — suggesting that new breeds are developed from crosses within specific breed groups that share particular traits," Wayne said. "If they want a new sight hound, they tend to cross sight hounds with each other, and the same with herding dogs and retrieving dogs. That may not seem so surprising, but we had no reason to think beforehand that these groups would be strongly genealogical.

"There are some notable exceptions, such as 'toy dogs.' In this grouping, there are many different kinds of lineages represented, including traces of herding dogs and retrievers. When it comes to miniaturizing a dog, breeders start with a larger breed and cross that with a miniature dog to make a dwarfed breed on a new genetic background, causing the mixing of various lineages. It's a mix-and-match approach for some of these breed groupings. But in other cases, new breeds have been based on combinations of breeds that have specific traits."

New insights into the evolution of dogs have emerged from this Nature paper and several other recent studies by biologists, including Wayne and his colleagues.

"A framework about dog evolution is emerging," Wayne said. "Even though dogs have an almost infinite variety of forms, geneticists have been discovering that much of this diversity has a simple genetic basis. Short-legged dogs — there are at least 19 such breeds, including dachshunds, corgis and basset hounds — have short legs due to the appearance of just one unique gene, a mutant growth-factor gene."

Recent research by Wayne and his colleagues has identified genes responsible for short legs, small size, different fur types and different coat patterns and colors.

"It seems that in dogs, unlike other domesticated species, many of these different phenotypes distill to just a handful of genes," Wayne said. "These genes have been mixed with retrievers, herding dogs and sight hounds to create new breeds."

In humans, by contrast, most differences in height and weight involve many genes, each of which has only a small effect; most of the genes account for only about 1 or 2 percent of variability. Even in agricultural plants, most genes have only a small influence on a single trait.

In dogs, however, one gene that is responsible for differences in size accounts for more than 50 percent of the variation in body size, Wayne said. A small number of genes, he said, have been moved around in dogs to create the appearance of amazing diversity.

"Because we analyzed 48,000 locations in the genome, we can ask which regions are the most different between dogs and wolves," said Novembre, whose research group investigated whether specific regions of the genome have changed under domestication. "We identified a few regions that are exceptionally different between dogs and wolves; these might be places in the genome where some of the changes occurred that make dogs and wolves different from each other today. These are good candidate regions for follow-up research."

In a separate paper, Melissa Gray, who earned her Ph.D. from UCLA in Wayne's laboratory, reported in February, along with Wayne and colleagues, on an important gene known as IGF1, which is responsible for small size in dogs, and analyzed which wolf populations are closest evolutionarily to this gene. The findings, published in the journal *BMC Biology* show that the gene appears to have arisen in Middle Eastern wolves, giving further support to the major claim in the new *Nature* paper.

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