Hi! We're scientists from the Ostrander Lab at the National Human Genome Research Institute, part of NIH, and we study dog genetics and their genomes. Ask us anything!

Ostrander$_{L}ab^{1}andr/ScienceAMAs^{1}$

[1]Affiliation not available

April 17, 2023

Abstract

What can research studies on man's best friend tell us about ourselves? As it turns out, quite a lot! That's exactly what we're doing as scientists who run the NHGRI Dog Genome Project. Dogs are a treasure-trove of information for understanding natural variation in populations. For example, within the 175 dog breeds recognized by the American Kennel Club (AKC), you can find many differences in how traits are displayed including body size, leg length, skull shape, or fur color and type. What are the genes driving the body size differences that we see between a Chihuahua and a Great Dane? Which genes contribute to the curly fur of a Poodle versus the bristly fur of a Wirehaired Pointer? Sequencing the genomes of each dog breed and comparing them allows us to determine the genes and changes in DNA sequence responsible for those outward differences. How does this work relate to us humans? While we don't have fur, we do have natural variation in outward traits, just like our four-legged friends. By learning more about them, we can help better understand ourselves in the process! In addition to the above, dog breeds vary greatly in their risk of getting certain diseases. More than 350 inherited diseases have been described in domestic dogs. Certain diseases occur with remarkably high frequency in small numbers of breeds, or in groups of closely-related breeds. This suggests these diseases may have a genetic component. Since many diseases in dogs are similar to disorders in humans, NIH studies of dog genetics provides insights into human diseases as well. In fact, NIH studies have been particularly successful at finding genes that influence cancer susceptibility and progression in dogs, and determining whether they function the same way in humans. The NHGRI Dog Genome Project is part of a world-wide consortium aimed at sequencing the genomes of 10,000 dogs within the next five years. About 1000 are already done! Our studies are all based on collaboration with dog owners and involve collecting DNA samples, health histories, and pedigrees. Your dog can be part of our research studies, too! We are always interested in the voluntary submission of DNA samples from all types of dog breeds as we continue to develop new studies every year. Check out our Facebook page (https://www.facebook.com/DogGenomeProject/) and NHGRI Dog Genome Project website (https://research.nhgri.nih.gov/dog_genome/) for more info. Ask us anything about dog genetics, and our work on natural variation in dog populations and human disease! Your hosts today are: Elaine Ostrander, Ph.D., Chief of the Cancer Genetics and Comparative Genomics Branch, Distinguished Investigator at the National Human Genome Research Institute. Dr. Ostrander's Border Collie, Tess, was one of the first dogs entered into the dog genome project. Heidi Parker, Ph.D., Staff Scientist, Cancer Genetics and Comparative Genomics Branch, National Human Genome Research Institute. Dr. Parker's dogs, Hattie and Grace, are accomplished competitors in barn hunt (rat hunting)! Fortunately, Hattie and Grace do not bring the rats home. Dayna Dreger, Ph.D., Senior Research Fellow, Cancer Genetics and Comparative Genomics Branch, National Human Genome Research Institute. Dr. Dreger owns several Shelties who have distinguished themselves with awards and championships in obedience competitions. Her dogs have won so many ribbons she's making them into quilts (the ribbons…not the dogs)! UPDATE: Thanks so much for asking all your great questions! We're all done for the day, but will continue to answer a few more questions as they come in! You're the best, Redditors!

the
WINNOWER

REDDIT

Hi! We're scientists from the Ostrander Lab at the National Human Genome Research Institute, part of NIH, and we study dog genetics and their genomes. Ask us anything!

OSTRANDER_LAB R/SCIENCE

What can research studies on man's best friend tell us about ourselves? As it turns out, quite a lot! That's exactly what we're doing as scientists who run the NHGRI Dog Genome Project.

Dogs are a treasure-trove of information for understanding natural variation in populations. For example, within the 175 dog breeds recognized by the American Kennel Club (AKC), you can find many differences in how traits are displayed including body size, leg length, skull shape, or fur color and type. What are the genes driving the body size differences that we see between a Chihuahua and a Great Dane? Which genes contribute to the curly fur of a Poodle versus the bristly fur of a Wirehaired Pointer? Sequencing the genomes of each dog breed and comparing them allows us to determine the genes and changes in DNA sequence responsible for those outward differences.

How does this work relate to us humans? While we don't have fur, we do have natural variation in outward traits, just like our four-legged friends. By learning more about them, we can help better understand ourselves in the process!

In addition to the above, dog breeds vary greatly in their risk of getting certain diseases. More than 350 inherited diseases have been described in domestic dogs. Certain diseases occur with remarkably high frequency in small numbers of breeds, or in groups of closely-related breeds. This suggests these diseases may have a genetic component. Since many diseases in dogs are similar to disorders in humans, NIH studies of dog genetics provides insights into human diseases as well. In fact, NIH studies have been particularly successful at finding genes that influence cancer susceptibility and progression in dogs, and determining whether they function the same way in humans.

The NHGRI Dog Genome Project is part of a world-wide consortium aimed at sequencing the genomes of 10,000 dogs within the next five years. About 1000 are already done! Our studies are all based on collaboration with dog owners and involve collecting DNA samples, health histories, and pedigrees. Your dog can be part of our research studies, too! We are always interested in the voluntary submission of DNA samples from all types of dog breeds as we continue to develop new studies every year. Check out our Facebook page (https://www.facebook.com/DogGenomeProject/) and NHGRI Dog Genome Project website (https://research.nhgri.nih.gov/dog_genome/) for more info.

Ask us anything about dog genetics, and our work on natural variation in dog populations and human disease!

Your hosts today are:

Elaine Ostrander, Ph.D., Chief of the Cancer Genetics and Comparative Genomics Branch, Distinguished Investigator at the National Human Genome Research Institute. Dr. Ostrander's Border Collie, Tess, was one of the first dogs entered into the dog genome project.

Heidi Parker, Ph.D., Staff Scientist, Cancer Genetics and Comparative Genomics Branch, National Human Genome Research Institute. Dr. Parker's dogs, Hattie and Grace, are accomplished competitors in barn hunt (rat hunting)! Fortunately, Hattie and Grace do not bring the rats home.

Dayna Dreger, Ph.D., Senior Research Fellow, Cancer Genetics and Comparative Genomics Branch, National Human Genome Research Institute. Dr. Dreger owns several Shelties who have distinguished themselves with awards and championships in obedience competitions. Her dogs have won so many ribbons she's making them into quilts (the ribbons…not the dogs)!

UPDATE: Thanks so much for asking all your great questions! We're all done for the day, but will continue to answer a few more questions as they come in! You're the best, Redditors!

READ REVIEWS

WRITE A REVIEW

CORRESPONDENCE:

DATE RECEIVED:
November 03, 2017

DOI:
10.15200/winn.150962.23453

ARCHIVED:
November 02, 2017

CITATION:
Ostrander_Lab , r/Science , Hi! We're scientists from the Ostrander Lab at the National Human Genome Research Institute, part of NIH, and we study dog genetics and their genomes. Ask us anything!, *The Winnower* 4:e150962.23453 , 2017 , DOI: 10.15200/winn.150962.23453

Good morning,

I was wondering that with being able to sequence these dog genomes to tell differences between breeds in various traits, is it possible to determine exactly how much of a breed is in a mutt and make an educated guess at their pedigrees?

LostinWV

Yes, it is indeed possible to identify the component breeds of a mixed breed dog using DNA sequence. By comparing the sequence of your mixed breed to hundreds of purebred dogs, whose sequence is readily available, we can identify both breeds of origin and percentages of founder breeds.

I'm curious whether the huge range of diversity in size between subspecies can give us some clues about loci that affect human height and weight. I would imagine given that they are both vertebrates, at least some of the responsible regions might share homology and dogs have gone through artificial selection based on size so many independent times, I feel like it might be easier to tease out the responsible loci in dogs than in human GWAS studies. Has this been looked at? thanks

thebuddhaguy

You are correct. The genes we have found that control variation between dog breeds, including body size, are important for controlling various aspects of human size and shape as well. Finding them in dogs, where many fewer exist, gives us a scaffold for organizing the hundreds of genes that control human height, weight, proportion, etc.

What is the furthest back known common ancestor shared by most/all modern domesticated dogs?

adenovato

Only one winner in that contest! The grey wolf. Actually, the ancestor of the modern grey wolf, now extinct, is likely the predecessor to both it and the dog.

Hi - certain breeds of dogs suffer diseases from inbreeding and general lack of genetic diversity. While I understand that this can be avoided through proper breeding programs, can any of the work that you are doing help prevent this from happening (perhaps through some form of a test required or certificate that can be requested from breeders)? I think it would be great if I could purchase a certified “disease free” dog, or maybe this is not possible prior to breeding. Vet bills can be very pricey.

BMonad

Much of our work involves identification of disease-causing or risk-associated variants for breed-specific diseases. While we don't market any of these tests commercially ourselves, the science is often picked up by commercial operations that will offer the tests to breeders and dog owners. So in that sense, yes, there are ways that breeders can test their breeding stock for various disorders prior to breeding and many breeders will offer pups from parents with known genetic results. Our understanding of dog breed relationships will continue to provide valuable information regarding potential disease-causing genetic variants in more breeds.

Oh hai! I'm going to ask you something that would be extremely unethical to do. Based on your research findings, could we breed humans to design an incredible diversity of traits like we achieved in dogs?

lucaxx85

Apart from the unethical attributes of this, there appears to be something special about the dog genome that allows it to hold a large amount of variation and allows for humans to select on distinct characteristics in a relatively short amount of time. This degree of phenotypic variation is not present in other species including humans.

I've read that the pheromones released between a mother and her child is similar to that of a dog and its master.

1) Why is this fact a fact?

2) Can a dog feel unconditional love towards any non-human?

3) A species should normally feel attraction in order to mate and reproduce. Why do dogs like humans then?

4) Can we untame a generation of dogs?

MasterAgent47

Hi, MasterAgent47! Great question?

1.) There was a recent study (https://www.ncbi.nlm.nih.gov/pubmed/29081760) looking at the levels of oxytocin and cortisol released in dogs and humans based on gaze. They found that looking at dogs causes a reaction in humans that might affect the relationship. Probably not the same as mother and child, but it’s still an interesting finding nonetheless!

2.) Dogs react to human faces in a way that they don’t react to any other species. Certainly stories exist where lost dogs will travel hundreds of miles to find their original owners. We don’t really know what emotion this is, but it clearly represents some type of attachment that dogs find comforting and desirable. We can’t say that this is love, but we like to think so.

3.) Since dogs are natural pack animals, we think they feel a more familial relationship with us than anything else. A species can have attraction to a species that it does not mate with. Consider cats, 'cause you know we won't :) . Also, there are lots of things that can make our dogs love us. Also, we have cookies!

4.) Dogs were domesticated a very short time ago, about 15-30 thousand years ago. Much of early breed development was driven by human selection for various traits, many of which were important for human survival including herding, guarding, and hunting. This also included selection away from traits associated with being “wild.” We don’t have any mechanism to unselect the fundamental nature of what makes a domestic dog or reintroduce wild characteristics. I have to admit I’m not sure we’d really want to make dog breeds wild. Do you really want to see a pack of wild French Bulldogs or Toy Poodles?

I think this is a great idea as in breeding is a way to improve the resolution of QTL mapping in other species! Unfortunately for us, humans have pretty long generation times and they usually object to the backcross 😄

I think that the morphological differences between dogs is fascinating, and the idea that there could be just a few repeated genetic motifs governing this is interesting. BUT what is coolest to me about dog breeds are their behavioral traits. This seems much much harder to quantify and map, but is the lab doing any work on this?

In a similar vein, is there any effort to sequence wild dogs (wolves) to understand the genetic factors that contributed to domestication?

To what extent do you think we won't be able to explain dog traits genetically and through regular NGS and need to look epigenetically?

In all of this, I imagine it's tough to separate causal mutations from passenger mutations statistically.. do you see any way, short of doing the actual careful genetic knock-ins, to improve the predictive power of your sequencing approach?

Do you have immortal dog cell lines??

Sorry for all the questions, I just had this same idea one day and I'm glad someone is doing it!

MichaelSwizzy

Hi MichaelSwizzy! Great questions!! Here we go!

1.) Many dog labs are interested in identifying genes that contribute to behavioral differences between breeds. You are right, though, that it is very hard to quantify behavior. Scientists are using other techniques to simplify the problem. For instance, by studying geographic origins of breeds we can divide dogs with similar traits into smaller groups that are more likely to share common genetics.

2.) There have been a number of studies aimed at looking for the early genetic contributions to domestication. Some compare wolf genome to dogs to identify the changes that are present in all dogs. Another interesting study looks at the recently domesticated foxes to understand what has been selected for and how that might relate to the dog story. (https://www.ncbi.nlm.nih.gov/pubmed/27757730)

3.) I think there is strong evidence at this point that a variation in dog breeds is controlled by many factors including variation in the coding part of the genome (exomes), DNA sequences that regulate expression of genes (promoters and enhancers), things that stabilize messenger RNA (poly A tails), as well as epigenetic, or other non coding factors such as methylation. The dog genome community has assembled a consortium from over 18 countries to sequence 10,000 canid genomes in the next five years. Along with that comes a goal of doing all the things you propose. Stay posted for those results and if you have an interesting dog to sequence, let us know!

4.) Causation is always difficult to prove. One of the ways that we address it is to look at multiple breeds with the same trait in order to reduce our associated regions to the smallest possible. We are also putting a lot of effort into identifying regulatory regions and how they work in order to better assign non-coding mutations.

5.) There are very few immortalized dog lines. Most, (might be all lines, up till very recently) are actually cancer cell lines that come with mutations which allow the cells to grow indefinitely, much like how tumors naturally grow.

Thanks for writing about dogs. The idea of understanding the genetics underlying the mammal with the greatest level of variation on the planet is exciting! I confess that's why we like dogs more than cats (sorry cat owners).

Are there breeds of dogs that are essentially "natural", i.e. they would exist without breeders?

greenvortex

The closest we could get to that answer would be to look at some of the feral dogs around the world. There are domestic dogs that exist within cities and towns worldwide, surviving from scavenging. While these populations have some influence from stray dogs of known breeds, they are primarily a free-breeding population of their own. Interestingly, they most often appear as mid-sized, short-haired, fawn or red in color, with slightly curled tails.

Hi! I did a mixed breed DNA test on my rescue dog and it was determined he was level one Yorkie Terrier. I phoned the lab and queried if there was any other breed identified in him as the dog is 19lbs. He is not overweight- frame matches weight but easily over double the standard size. It was explained that at a minimum both his parents were 50% purebred and he only inherited 100% yorkie genes from them. 50% from Mom 50% from Dad. Does this sound correct? Is there a scientific explanation as to why he is so much larger?

Note- we don't care if he's a purebred just curious how he ended being a Yorkiesaurus. There isn't a visual clue of any other breed mixed with him.

daftvancitypunk

Hey, thanks for the question. There are a number of factors that could come into play here. While the breed standard lists certain heights and weights, that doesn't mean that all dogs of that breed will meet those levels. There are plenty of oversized or undersized dogs of most breeds. Also, we have identified at least nine major genes so far that contribute to dog size, with likely many more genes undiscovered. Those genes in different combinations can tweak the size higher or lower than "ideal". However, I would be suspicious of the explanation that, while each parent is 50% Yorkie, your pup somehow got 100% of the Yorkie genes. That part doesn't seem accurate.

Hi quick question, How many homo .... s (ya know, like homosapien) does science know about??

pleasedont300219

So we assume you mean how many species are in the genus homo? We know of several, and the scientific literature defines them really well and new ones are being identified all the time. I have to say our area of interest is dogs. There are nine species of Canis, 10 if you include the dog as a distinct species rather than a subspecies. There are over 400 breeds of dog, and new breeds are introduced every year; however, all breeds are of the same species.

Were you able to sequence the good boy gene

mihaeagle3

So I know your question was probably meant in humor (I liked it), but there is an interesting paper that just came out in Science Advances which describes a gene region associated with sociability which was selected during domestication of dogs from wolves. When deleted in humans, the same gene region is associated with a condition called Williams-Beuren Syndrome. One characteristic of the human syndrome is extreme sociability. So while this is not the "good boy" gene, the result really speaks to the fact that we can find genes associated with dog behavior that are relevant for human conditions as well. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5517105/

What breeds are you most interested in sequencing, if you can get a sample? If you have all sequenced your own dogs, did you find any surprises?

TelemarketingEnigma

Thanks for the great questions! Ultimately, we are interested in sequencing all breeds of dogs! Our lab started with the American Kennel Club Breeds, and investigators worldwide are sequencing hundreds of other breeds. We've come together as a community to develop a project called DOG10K, which has a goal of sequencing 10,000 canines over the next 4 years. If you have an interesting breed, let us know. We'd love to add it to our dataset.

To answer your second question, those of us with breeds that were eligible (had pedigrees) were added to the dog genome project. No special surprises, but each and every dog contributes data and ultimately knowledge to the project.

Does where you collect the dog DNA (so say Finland versus the US) create any difficulties in analysis? Does a particular breed in Finland have the same basic genes as in the US or is it slightly altered to help the dog in the different climate? Do you have to account for any bias from people who send in the DNA? For instance, their dogs might be sick so they want to help where as someone with a healthy dog might not contribute? I dont know much bio so replace words until my questions make sense XD

RattieRatRatRat

Because most breeds in the United States were originally imported from another country, they have gone through a bottleneck that reduces genomic variability. We can see this in our analyses and often have to make corrections for different geographic regions or even separate the populations if the difference is very large. So far we have not seen a huge bias toward sick dogs in our DNA collections, unless we are deliberately seeking dogs affected with a disease such as cancer, because we often target shows where there are lots of very healthy dogs. This does seem to be an issue for survey data collection and is always something we keep in mind. You can find a list of current studies on our website: https://research.nhgri.nih.gov/dog_genome/study_descriptions/index.shtml

How are you obtaining the DNA for this project? Can I send my pup's DNA to you?

cooptown03

Great question, cooptown03! ;) All of our DNA samples come from blood or saliva samples collected from pet dogs around the world. Owners contact our samples manager and if their dog is eligible for one of our studies we will get their dog enrolled. We mail each owner a kit that has everything their vet needs to collect the sample including test tubes, an information sheet and, of course, a consent form for the owner to sign. If you are interested in donating a sample to the Dog Genome Project, please email us at dog_genome@mail.nih.gov and we'll chat with you, learn more about your dog, and send you a collection kit!

Hello, I would like to ask of there is any scientific basis to the claims that some dog breeds are smarter than others. If there is, would that mean that genetics really do directly influence intelligence? Thank you

NephthysSekhmet

This is a complex question that many researchers have attempted to answer. Most of the resources out there associate intelligence with trainability, or the willingness of a dog to do the things you ask it to do. But as we all know, there are many ways to be smart. Some breeds will figure out how to unlatch the gate to your yard, but will be reluctant to learn to fetch. There are certainly breeds that excel at working with humans and following their directions, while other breeds are independent workers, not relying on human direction. In that sense, since we can classify those behaviors to breeds, it is reasonable to attribute a genetic component.

I am curious specifically about Malamutes and other Northern breeds concerning their issues with zinc. I was curious where the location of zinc deficiency would be located and if there is a test out there that could be done to prevent this condition from causing the problems it does in these Northern breed dogs?

Ferelwing

At this time we are not aware of a test for zinc-responsive dermatosis but there are studies assessing the effectiveness of zinc supplementation as a treatment (www.ncbi.nlm.nih.gov/pubmed/?term=11360336). Cases like this, where there is increased risk of a specific and uncommon disorder in a small number of closely related breeds, are perfectly suited for a genetic study because the culprit is likely something inherited from the common ancestor of the affected breeds.