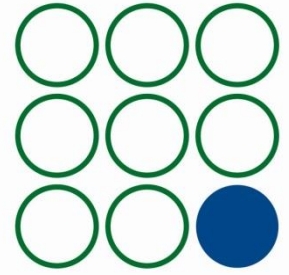




THE KENNEL CLUB

GENETICS CENTRE

AT THE ANIMAL HEALTH TRUST



Give a Dog a Genome – FAQs

How will you select the dog to represent each breed?

There are various criteria we can use to select a dog. We might choose a dog that is affected with an inherited disease, or we can select an older 'apparently healthy' dog with no known inherited conditions, that has had a full eye examination. This will strengthen its use as a control for the many studies of inherited eye diseases that we conduct at the Animal Health Trust.

If a dog is affected for a simple inherited condition (a condition caused by a single gene mutation), the vast majority of its genome will be comprised of a wealth of common neutral differences, or variants, and this applies to all dogs. This means that the genome sequence of any dog can therefore contribute to the bank of genomes as a resource to act as a normal 'control' for other breeds.

How can a single dog's genome represent a whole breed?

The simple answer is that a single dog cannot represent a whole breed. The strength of our collection of whole genome sequences will come from the collection as a whole, with each individual genome adding incremental power to the canine genome bank. When we compare the genomes of two dogs we find about 2-3 million places in the DNA where the sequence is different. Most of these differences are neutral variants that probably have no or little effect on the dog's health and function.

The more breeds that are represented in the genome bank the greater the chance we will find each variant more than once and will therefore be able to assign it as a common neutral variant. In an ideal world we would sequence the whole genomes of large numbers of dogs of each breed – but this would be prohibitively expensive. The next best thing is to have a bank of genomes of dogs of different breeds, the sum of which should enable us to designate many common neutral variants, while spreading the cost across multiple breeds.

How will you use this bank of whole genome sequences in your research?

When we compare the genome of an affected dog with the reference genome (or the genome of another apparently healthy dog) we will find about 2-3 million places in the DNA (out of around 2.4 billion) where the sequence is different between the two dogs. One or more of these differences, or variants, might be a disease-causing mutation, but the total number is obviously far too many to realistically investigate, so we need to filter out the variants that are benign, or neutral.

One way to do this is to look in the genomes of other dogs to see if the variants are shared by other dogs, or are 'private' to the affected dog, or its close relatives. If we find a variant in another dog, of another breed for example, that does not have the same disease we can exclude that variant as being the cause of the particular condition we are investigating.

How can you avoid the dogs that are sequenced carrying disease mutations themselves?

We can't, which is why during our research we typically exclude genomes from the same breed as the affected dog that we are investigating. We expect that most mutations for diseases with a simple pattern of inheritance are more or less private to specific breeds. So, for example, if we were looking for the mutation that causes a disease in Irish Setters we would compare the genome sequence of the affected Irish Setter with the genomes of as many other breeds as we could, but not include any Irish Setters or related breeds in that initial comparison. If we find a variant in another dog that does not have the same disease, we can exclude that variant as being the cause.

The more genomes we have to compare with the affected Irish Setter's the greater our chances of filtering out all the neutral variants to leave us with just the causal mutation. The more variants we can filter out using this approach the quicker and cheaper the research will be.

How does a breed register its interest in participating in the Give a Dog a Genome project?

The Breed Health Co-ordinator (BHC) of any interested breed should email us on gdg@aht.org.uk to register interest.

As we already have 75 breeds participating in Give a Dog a Genome, their breed will then be placed on the waiting list for GDG2, which is expected to begin in 2018. Once we have secured funding for GDG2 we will contact all the breeds on the waiting list, and they will be given approximately four weeks to confirm their willingness, by email, to participate and make the required donation of £1,000 at which point we will then discuss potential candidate dogs and provide details of how to make the payment.

How should the donation be made to the AHT? Can it be made online?

The easiest way to make the donation will be via cheque or bank transfer. Once your breed representative has secured the place on the GDG waiting list, via emailing gdg@aht.org.uk or calling 01638 751000 Ext: 1274, more information on how to make the donation will be provided via email.

How many breeds will you be able to sequence a genome for?

The KCCT has pledged £75,000 for whole genome sequencing. This amount will enable us to match donations of £1,000 from 75 breeds and thus sequence the genomes of 75 different breeds.

What happens if more than 50 breeds wish to donate £1,000?

The 75 breeds we can sequence with the KCCT's current funding (plus the matched donations from breeds) will be selected on a first come first served basis. We will use the KCCT funding to sequence the genomes of 75 different breeds. The breeds which do not make the list of 75 breeds will be placed on the waiting list for the second phase of Give a Dog a Genome (GDG2), which is expected to begin in 2018.

Can our breed donate £2,000 to guarantee a whole genome sequence for our breed?

Yes, if any breed chooses to donate £2,000 we guarantee to sequence the genome of a dog of their breed in addition to the 75 breeds already participating.

If a breed donates more than £1,000 can more than one dog be sequenced?

Yes. We will allocate a maximum of £1,000 from the KCCT funding to each breed but breeds are welcome to pay £2,000 for each additional genome. For example, if you are one of the first 75 breeds to contact us, we will be able to sequence one dog of your breed for £1,000, two dogs for £3,000, three dogs for £5,000 etc. If the first 75 genomes have already been allocated, you will need to donate £2,000 for the first and each subsequent genome.

What about breeds that are not able, or choose not, to participate?

We obviously can't make breeds take part, and we certainly wouldn't exclude a breed from benefitting from the genome bank even if they hadn't participated. But the more breeds that are represented in the genome bank the more powerful it will be.

Will the identity of dogs be kept confidential?

The AHT will not reveal the identity of any dog whose genome is sequenced and we might collect DNA from more than one suitable candidate with the final selection being made solely at the discretion of the AHT. Anonymous sequence data may be shared with

scientists from other institutions when doing so is considered to be in the best interests of research.

How will each participating breed be kept updated throughout the project?

We will conduct all communications via the Breed Health Co-ordinator (BHC), on the expectation they disseminate the information appropriately to all relevant parties. We will inform the BHC when DNA from their breed has been sequenced and added to the genome bank, and also if/when any breed-specific findings are made.

Give a Dog a Genome Timeline:

- **Registering interest – COMPLETED**
The 75 breeds that will receive KCCT matched funding will be assigned on a first come first served basis. Once a Breed Health Coordinator (BHC) has emailed to register their interest, that breed will be added to the waiting list to temporarily secure the KCCT funding while the £1,000 donation is raised.
- **Confirming interest – COMPLETED**
Once a BHC has registered interest in the Give a Dog a Genome project they will be given approximately four weeks to confirm their breed's interest, at which point they will be assigned a confirmed position on the waiting list, subject to receipt of £1,000 by a specified date.
- **£1,000 donation – COMPLETED**
The Breed Health Coordinator, or someone appointed by them, will then have at least three months to coordinate or raise the £1,000 donation, or update the AHT of their donation progress to maintain their breed's place on the list.
- **After donation is received – ONGOING**
Once the donation has been received the AHT will liaise with breed representatives to identify possible candidates for the whole genome sequencing. DNA will be submitted in the normal form of a cheek swab sample from at least two or three candidate dogs.
- **Genome sequencing – ONGOING**
The identity of the dog whose DNA is sequenced will be kept strictly confidential by the AHT. The BHC will be informed when the genome has been sequenced and if there are any significant results straight away. Certificates to mark this contribution will also be issued, if required.
- **Updates – 2016 and 2017**
Throughout 2016 and 2017 the AHT will be issuing updates on the progress and developments of Give a Dog a Genome via the AHT news page, press releases, and a dedicated GDG email list. If you would like to receive email updates, [click here](#).
- **2018 –**
Review of breeds sequenced and what we've learnt in phase 1 of Give a Dog a Genome. Initiation of phase 2.