Finding the Genes that Determine Canine Behavior

The following is an explanation of how scientists working on the Dog Genome Initiative set out to identify genes that determine behavior or inherited diseases in dogs. Research methods have evolved to include other approaches in the 15 or so years since then, but this remains a good explanation of genes and gene mapping. It was written for non-scientists by Dr. Polly Matzinger, an immunologist and sheepdog handler.

Start by thinking of GENES as pearls on a string (made of DNA instead of oyster saliva).

O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-0-O-O-

Dogs, like people, have lots of these strings, a bit like a multi-strand pearl necklace. The strings are called chromosomes. Now suppose that you wanted to know how many of these genes it takes to control something as complicated as the behavioural trait we call “eye” and you wanted to know which particular ones, on which particular strings, do the job. If you look at the chromosome strings in a microscope, they all look pretty much the same, though some are longer than others.

O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-0-O-O
O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O
O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O

Suppose that the third gene on the first chromosome string has something to do with the INTENSITY with which an animal pays attention to an object, the 11th gene on the second chromosome controls whether it pays attention by LOOKING rather than listening or smelling, the 7th gene on the third chromosome controls HOW LONG it will continue to pay attention, and the 22nd gene on the 4th chromosome controls whether it pays attention to STATIONARY or only moving objects.

1 O-O-(I)-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-0-O-O-O-O-O-O-O-O
2 O-O-O-O-O-O-O-O-O-O-(L)-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O
3 O-O-O-O-O-O-(HL)-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O
4 O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-(S/m)-O

How would you ever be able to find this out? remember, the chromosomes all look the same.

This is NOT an easy task and for years we didn’t have the technology to do it, but recently several interesting and odd quirks of nature have been discovered that open the way.

One of the odd quirks is a type of DNA called ‘micro-satellite’. These are funny little areas where the DNA string can stretch and contract. They are a little like the leaves of a dining table that can

be used to make it longer. The micro-satellite extensions are always made of the same stuff but sometimes they are very long (a boardroom table, lots of extensions added) and sometimes short (a card table). There are about 4,000 of these in most species that have been studied and they are scattered all around the genome (another word for the total number of strings that make up the pearl necklace). So our picture of the DNA pearl necklace begins to get a bit more detailed:

1 O-O-(I)-mmmmmmmmmm-O-O-O-O-mmmmm-O-O-O-O-O-O-O-mmmmmmm-O-O-O-O-0-O-O-O-
2 O-O-O-O-O-O-O-O-O-mmmm-O-(L)-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmmm-O-O-O-O-
3 O-O-O-O-O-O-(HL)-O-O-O-O-O-O-mm-O-O-O-O-O-O-mmmmmm-O-O-O-O-O-O-O-O-O
4 O-O-mmmmmmmmmmm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmm-O-O-O-(S)-O

No one really knows why the micro-satellites exist, but the current view is that they are due to slippage mistakes made during the repair of the strings, which, being very delicate, periodically break and need repair. The micro-satellites have three properties that make them incredibly useful to researchers who want to find the genes that control particular traits.

First, because the micro-satellites are always made of the same stuff, they can be located and mapped. For example, chromosome number one in dogs (the chromosomes were originally numbered in order of length, since there was no other useful way to tell them apart: number one is the longest) might contain a micro-satellite 1,000 units in from the left end, and another one that is 450,000 units further down to the right and so on. People have been working on the micro-satellite maps of the chromosomes of different species for a couple of decades and some of the maps are getting very close to complete.

Second, their lengths will vary randomly, so the one that is 1000 units in from the left end might be 92 units long, whereas the next one down might only be 31 units long and so on. Each micro-satellite therefore has two properties that identify it; its position and its length (like mapping the co-ordinates of a city and also knowing its size)

Third, the more distantly related two individuals are, the more different their micro-satellites will be. Breaks in dog strings, for example, will be randomly repaired differently from those in human strings, not because there's anything inherently different about dog DNA but simply because the breaks are random. So, although both humans and dogs carry genes for blue and brown eyes, and red and black hair (and probably for behavioral things like attention spans and ability to see and hear), the years of breaks and repairs that have gone on between us will lead to differences in the positions and lengths of the micro-satellites

Border collies and newfoundlands, though not as different as humans and dogs, have been separated for long enough that many of their micro-satellites are different. So people like the

Dog Genome researchers can look at the micro-satellite map of, say, chromosome two and know whether the chromosome came from a border collie,

2b O-O-O-O-O-O-O-O-O-mmmm-O-(Lo)-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmmm-O-O-O-O-O-O

or a newf,

2n O-O-O-O-O-O-O-O-O-mmmmmmmm-O-(li)-O-O-mmmm-O-O-O-O-O-O-O-O-O-O-O-mm-O-O

just by looking at the micro-satellites.

I'm making a couple of assumptions here. In the position where the border collie has the gene for paying attention by looking (Lo), I'm assuming that the newf has a gene for paying attention by listening (li). This may not be true, of course, but let's use it for illustration. The same sort of thing holds for chromosome four, where sits the gene for paying attention to stationary things or to moving things. Lets say that the border collie has a gene that induces it to pay attention to things regardless of whether they are moving or stationary (a scared sheep? The sheep that's been backed into a corner?), while the newf mostly pays attention to things that are moving (drowning people rather than the rocks their boat crashed on). So at position 22, the border collie chromosome has the stationary/moving gene (Sm) and the newf has the moving gene (m). The two chromosomes will also have different micro-satellites.

border collie

4b O-O-mmmmmmmmmmmm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmm-O-O-O-(Sm)-O

newfoundland

4n O-O-mm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmmmmmmm-O-O-O-(m)-mmm-O-

Now remember that nobody knows where the behavior genes are (or even how many exist, or which types of behavior are influenced by genes). They only know the positions and lengths of the micro-satellites. How can they use this information to find the behavior genes?

They start by mating a newfoundland to a border collie. Now, in every individual, each one of the chromosome strings is actually paired up. There are two copies of each chromosome, one received from the mother and one from the father. So the border collie and the newf each has a pair of chromosome 2s and a pair of chromosome 4s. In the process of making eggs and sperm, they split these pairs up and donate one half (a complete set of singles) to all their progeny. All the puppies will thus have one set of chromosome strings from their mother (the newf, in this case) and one from their father. So their sets of chromosomes 2 and 4 will look like this.

2b O-O-O-O-O-O-O-O-O-mmmm-O-(Lo)-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmmm-O-O-O-O-O-O
2n O-O-O-O-O-O-O-O-O-mmmmmmmm-O-(li)-O-O-mmmm-O-O-O-O-O-O-O-O-O-O-O-mm-O-O

4b O-O-mmmmmmmmmmm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmm-O-O-O-(Sm)-O
4n O-O-mm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmmmmmmm-O-O-O-(m)-mmm-O-

By analyzing the behavior of this first cross, the scientists can make some guesses about the relative strengths of the different behavior genes, (though they won't yet be able to say how many there are or where they sit on the chromosomes). For example, if the puppies tend to look rather than listen, then looking (Lo) would be said to be DOMINANT over listening (li). If they tend to do both, paying attention with both their ears and their eyes, the genes would be said to be CO-DOMINANT. For the sake of this example, let's say that they are co-dominant. Lets also say that the Moving vs. Stationary genes on chromosome 4 are not co-dominant, but that paying attention only to moving things is dominant over paying attention to both moving and stationary things. So the puppies of a newf by border collie cross would pay attention only to moving things and they would do it by both listening and looking.

Good. This means that the first generation has taught us something, but not a whole lot. To learn more, we need to do some more breeding. We do this by breeding the puppies to each other (brothers to sisters) to make the second generation (called the F2 generation). Each parent will split its pairs of chromosmes, sending one copy (either the border collie copy or the newf copy) into the sperm or egg. The splits happen randomly so that a border collie type of chromosome 2 might end up going into the same egg as a newfoundland type of 4 etc. The puppies will therefore get all sorts of combinations of pairs of chromosomes. (Just like the progeny of a tri-color, prick eared bitch and a black, drop eared dog will come out in all the combinations of tri-color-drop eared, black-prick eared etc). Now things begin to get really interesting. We wait for the new puppies to grow up and then test them for the looking vs listening type of attention as well as for moving vs stationary attention. (The tests haven't really been worked out yet. In fact, I think this is the most problematic part of the whole project, but that's another story. Let's pretend that good tests have been devised and let's get back to the genetics, because the genetics will work for any trait, including many of the diseases for which good tests already exist).

Suppose that we find an F2 puppy that Looks (and doesn't listen) at both stationary and moving things. This is a dog that has copies of the border collie genes for LOOKING and STATIONARY/MOVING and doesn't have copies of the newfoundland genes. We don't know where these genes are yet, all we know is that we have found a dog that has them. So we take a little bit of blood, isolate the DNA from the white blood cells and look at the micro-satellite map. We find that both copies of chromosome 4 have a border collie type of micro-satellite pattern. We also find that both chromosome 2s are border collie type.

2b O-O-O-O-O-O-O-O-O-mmmm-O-(Lo)-O-O-O-O-O-O-O-O-O-O-O-O-mmmmm-O-O-O-O-O-O
2b O-O-O-O-O-O-O-O-O-mmmm-O-(Lo)-O-O-O-O-O-O-O-O-O-O-O-O-mmmmm-O-O-O-O-O-O

4b O-O-mmmmmmmmmmm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmm-O-O-O-(Sm)-O
4b O-O-mmmmmmmmmmm-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-O-mmmm-O-O-O-(Sm)-O

But we can't yet conclude that the Looking and Stationary/Moving genes are on chromosomes 2 and 4 because this dog also has two sets of border collie chromosomes 7, 9 and 13. Though these chromosomes don't carry any genes that we're interested in, we don't know that yet. All we know is that chromosome sets 2,4,7,9 and 13 are pure border collie. Let's say that sets 5,6 11 and 14 are pure newfoundland and all the rest are mixed pairs, where one comes from the border collie and the other from the newf. We can therefore guess that the LOOKING gene (Lo) and the gene for STATIONARY/MOVING attention (Sm) are somewhere on chromosomes 2,4,7 9 or 13.

To pin point it a bit closer, we need to find other dogs that have the border collie trait. Suppose that we now find one that looks (and doesn't listen) but only to moving things. We know therefore that it has the border collie Looking gene (Lo) and the newfoundland moving gene (m). When we analyse the DNA from its white blood cells, we find that chromosomes 1,2 and 7 are pure border collie, 4, 8, 9 and 15 are pure newf and the rest are mixes. We're now down to two choices for the Looking gene!! It must be either on chromosome 2 or 7 because these are the only two that are pure border collie in BOTH dogs. We haven't learned anything more about the Stationary/moving gene because this dog has the dominant trait (looking at only moving things) that can result from having either two pure copies of newf genes (m) or one copy each of the border collie (Sm) and the newfoundland (m) gene.

So we look at more dogs, hoping to find some more that have the Looking trait. We test them, find the ones that have the Looking trait rather than the Listening trait, bleed them, look at their DNA and . . . eventually . . . after a LOT of work, we pinpoint the Looking (and the Listening) genes to chromosome 2.

We've now accomplished the first step. We have mapped a behavior gene. We have learned a LOT from this. First, that there really is a gene involved in controlling this behavior, in the same way that there are genes governing ear prick and coat color. We've learned that a single gene is at work (not always true) and that it is co-dominant with its partner, the Listening gene. This means that, if we want dogs that will both look and listen, we'll need to keep making hybrids (like tomatoes) because this is a trait that needs both genes and therefore will never breed 'true'. Every time we breed two looking/listening dogs together, we will get some puppies that look (about one fourth of them), some that listen (another fourth) and about half that do both.

Now, please remember that this is a concocted fantasy example. I don't think that anything is known yet about the number, position, dominance, co-dominance or recessiveness of genes for behavior. I have just given an account of how the search is being done.

I think we can pretty well say that genes for behavior do exist. Anyone who has worked with different breeds of dogs can't help but know this. And hopefully, if these amazingly dedicated people get enough funding to do the work, we'll know the answers to some of our questions some day.