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Episode 9: Doggy DNA

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VOICEOVER
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SHANE HUNTINGTON
Hello and welcome to Up Close, coming to you from Melbourne University, Australia. I!|m Dr Shane Huntington and today!|s topic is Canine DNA. We!|re joined by Dr Steve Holloway. Steven is currently a senior lecturer in small animal medicine at the University of Melbourne, and we welcome him to Up Close today. Hello Steven.

STEVEN HOLLOWAY
Thank you very much, Shane.

SHANE HUNTINGTON
Now first of all you !V you lecture in particular in small animal medicine. I!|m trying to work out what!|s meant by small? In !V in that context, so horses I guess are out.

STEVEN HOLLOWAY
Yes, horses are not considered a small animal. I guess some people would call them companion animals. Most people would know them just plainly as dogs and cats, most of the time.

SHANE HUNTINGTON
Right.

STEVEN HOLLOWAY
It does include things like rabbits that might be classed as a small pet as well. Not horses, cows or sheep. That !V that sort of thing.

SHANE HUNTINGTON
Now, you!|ve !V you!|ve focused in - in particular on canines !V on dogs. Why !V why the choice there? Of all the amazing animals that, I guess, would!|ve come into your

clinical environment you !V you picked dogs.

STEVEN HOLLOWAY
Couple of reasons. First of all, I love dogs. I have a dog myself. And probably the pinnacle of what we know in terms of science would be of all the domesticated species would be in dogs, much more so than say horses or cows. And dogs are also !V I find them probably the most human of the pets. Yeah, I!|m a big dog fan, so.

SHANE HUNTINGTON
As a dog breeder myself, you are preaching to the choir here, I definitely agree that dogs are probably the most human and I have the bruises to prove it. There !V there are a lot of afflictions though that affect dogs in particular and !V and !V and those of us who do have a lot of dogs have a big !V often had a big bill associated with keeping them healthy. What !V what sort of afflictions do you deal with on a day to day basis, as a clinician with dogs.

STEVEN HOLLOWAY
I !V I work mainly in the medical field rather than the surgical field, but !V and this is what sort of stimulated my interest. We deal with a lot of cancer, very similar cancers to what people get. We deal with a lot of what we call autoimmune diseases where the immune system attacks oneself or the body for aberrant reasons, it makes a mistake and it turns on, for example, a common disease is to start making antibodies against your own red blood cells. That can be life threatening. We have to use large doses of cortisone to treat that.

SHANE HUNTINGTON
Before we get onto the immune system, I guess, with dogs, because we !V I want to get right into that at some stage. What sort of things can we control with breeding. So obviously, you know breeders will try and, I guess, get the best example of a particular breed available for the consumer and there are some things that we can control. What sort of things can breeding control you know just by knowing the bloodlines of the dog?

STEVEN HOLLOWAY
That!|s a very good question. Breeding!|s a double-edged sword. When you breed for a certain appearance which we call a phenotype, then you can get certain characteristics that you might find favourable. So for instance, I have a golden retriever, they!|re very good hunting dogs, they!|re very good companions, they tend to have a very gentle personality, they like to swim. The trouble is if you !V you breed them too closely, you may actually begin to breed in defects and breeders are very sensitive to that kind of thing. So [for] example, a common one that we screen for is hip dysplasia which is basically the ball and socket joint of the hip becomes flattened and it leads to arthritis very early in life. It!|s expensive and not very satisfactory to treat. And so, breeders go to a lot of trouble to x-ray the parents of the dog!|s hips, to make sure they!|re not affected by it before they breed with them. When we look at certain breeds of dogs, and I think, English bulldogs would be a good example, the !V the loveable pushed-in face that you know we find so attractive also is associated

with certain problems with breathing as well.

SHANE HUNTINGTON
Right.

STEVEN HOLLOWAY
Long soft palettes. So, you can go too far sometimes. And, that!|s the down side of breeding. Now, what we know now about dog breeds is that they!|re very closely related, all the individuals in !V in one breed if you look at them by genetic means. And this isn!|t the natural situation that would happen in the wild if you !V I went to Nepal trekking for example, and all the dogs there are basically cross bred dogs. They!|re very hardy dogs !V

SHANE HUNTINGTON
I would assume that those sort of genetic health problems and so forth that are coming through are !V are more likely in particular breeds as compared to a group of dogs that has been cross bred and cross bred and cross bred, is that exactly the case?

STEVEN HOLLOWAY
Yeah, I guess breeders would argue with you that you know when you buy a dog that!|s a cross bred dog, you really don!|t know how it!|s going to turn out personality wise and appearance, when it!|s a puppy. Whereas if you buy say a Siberian Husky you know very well what it will look like when !V when it!|s older you know.

SHANE HUNTINGTON
Yeah in fact I think in !V in breeding you often - to a degree predicting the outlook of the puppies from the parents.

STEVEN HOLLOWAY
Exactly.

SHANE HUNTINGTON
Now what about like, I guess, infectious agents in dogs. I mean, do we know much about that relative to humans?

STEVEN HOLLOWAY
We do, in fact infectious diseases are very well studied in animal patients, in general. This is probably because they!|ve been easier to study than, say, the other half of it which is the host response to the infection. So, dogs get streptococcal infections like people do, they get fungal infections. There!|s sometimes are different species that affects the dog !V

SHANE HUNTINGTON
Yep.

STEVEN HOLLOWAY
- but, and typically there is very great similarity between the types of infections. And

then, there!|s the subtle differences, like dogs don!|t get colds, for example. They don!|t get rhinovirus, for example.

SHANE HUNTINGTON
!K that!|s amazing isn!|t that they don!|t !K

STEVEN HOLLOWAY
Yeah, they get things that look like colds but they don!|t typically get the cold virus. Until recently, we didn!|t think they got influenza either. But now, dogs have actually been known to get influenza in America.

SHANE HUNTINGTON
You!|re listening to Melbourne University Up Close, I!|m Dr Shane Huntington and I!|m speaking with Dr Steve Holloway about canine DNA. Now Steve, let!|s move now into the immune system in general. So, before we get onto the canine aspect of it, tell us a bit more about the role it plays in !V in any animal.

STEVEN HOLLOWAY
Again, that!|s another good question. In any situation we like to look at in a holistic approach. We have the animal, its environment and its environment contains infectious agents etc. And so, we!|ve always been able to look at the infectious agents by culture or microscopy but we !V we haven!|t been able to see what makes the animal more susceptible to it. And we know !K in people, and we know in animals now that some animals and people are more susceptible to certain infections than other people. And, till probably the last 25 years we haven!|t been able to look at the immune system that easily in people or animals. But with the sort of human genome project and advances in immunology, we!|re now starting to be able to look at the host-parasite relationship or the host-infectious agent relationship, from the host!|s point of view, rather than just the infectious agent point of view. And that!|s kind of a bit of what my research is about.

SHANE HUNTINGTON
Following on from that, the !V the dog genome is !V is done as well isn!|t it? So !V

STEVEN HOLLOWAY
Yes, it is !K

SHANE HUNTINGTON
What !V what have we learnt from !V from that to date, I mean it!|s relatively recent?

STEVEN HOLLOWAY
We!|ve learnt that on a basic level we!|re very, very similar. Obviously, the chimp genome's the closest one that!|s been fully sequenced to the human one, but people!|d be surprised that dogs are around 95, 96% similar across the whole genome. And you know, what we!|ve learnt is that there!|s a lot more similarity than there is difference except in our !K appearance which is only probably a handful of the genetic information. Many of the diseases, for example, that have a genetic basis in !V in humans now we can say, !!!OWell maybe they!|ve the same genetic basis in

dogs.!!L
It!|s got a !V a !V an interesting aspect to it !¢FDcause we can now look across species to get clues about why some things happen in one species and don!|t happen in another.

SHANE HUNTINGTON
I mean, we even see behavioural differences coming in with the genetics as well in terms of you know, in my case, we have Siberian Huskies, they are bred to pull and run and if you let them off the lead you!|ll see that part of their !V their genome coming out very strongly, whereas other dogs are bred to guard and hunt and !V and whatever, and !V and it!|s a very specific aspect of that particular breeding.

STEVEN HOLLOWAY
Absolutely!K It's the reason why people don!|t have Golden Retrievers as guard dogs, for example.

SHANE HUNTINGTON
Exactly.

STEVEN HOLLOWAY
They!|re just !V they!|re !V they!|re not suited to it from their personality and so clearly there!|s behaviour genes there as well.

SHANE HUNTINGTON
Even that small percentage difference between the dogs is having a major impact on the diseases they get, the way they act and the way they look.

STEVEN HOLLOWAY
Absolutely. And so, we!|ve been looking at just one or two small areas to start with. Our research is focusing on immune response genes and it!|s based on some work that we done overseas by Dr Lorna Kennedy in Manchester. And, she was one of the first people to !V to start looking at these things in dogs. And we!|ve had conversations with her and now we!|re looking at Australian dogs too.

SHANE HUNTINGTON
Right.

STEVEN HOLLOWAY
And one !V one disease we!|re particularly we!|re interested in is a !V a rather nasty neurological disease that Maltese Terriers get for example, and I see them all the time in the clinic. This disease is sort of characterised by the immune system attacking the brain of the dog and the dog!|s come in, in a bad way with !V with it. The only treatment we can offer people is you know high doses of cortisone for example, immune suppressive drugs. So, we!|re looking to try and determine if some of these immune response genes are linked to that disease. So that the !V the dogs have a pre-disposition to that disease when they!|re born.

SHANE HUNTINGTON

Right.

STEVEN HOLLOWAY
And they come along and they get a triggering agent, and they make a mistake and attack their own brain, you know.

SHANE HUNTINGTON
In !V in some breeding I guess there are aspects of it that are what we!|d call recessive? Tell us a bit about that. I mean, this is not something you can necessarily look at the animal and say it has these particular features, I shouldn!|t breed it.

STEVEN HOLLOWAY
Well, recessive genes are genes you carry but aren!|t expressed outwardly, what we call phenotypically. And I guess Mendel worked this out some hundreds of years ago that you could take two non-affected individuals and the result of their progeny would be an affected individual. And those people are said to carry a recessive gene. If you get two copies of a recessive gene, one from your mum, one from your dad, then it!|s likely that you!|ll have the disease, because you don!|t have a good copy of the gene to make up for the bad one that!|s !V

SHANE HUNTINGTON
Right.

STEVEN HOLLOWAY
- and so, that!|s well known in human medicine for example and it!|s also known in canine medicine. Just by looking at the population as a whole you can start to see, well, this dog!|s likely to be a carrier. A classic example in dogs was worked out at the University of Melbourne by Professor Bruce Parry. We used to have haemophilia in German Shepherds in Australia, and as a young age, they would be just like haemophilia-A in humans, they would bleed profusely, which is a very bad thing.

SHANE HUNTINGTON
And !V and did that affect both the male and female dogs?

STEVEN HOLLOWAY
No, only males. And so the females carried it as a recessive gene, and the reason is that it!|s carried on the X chromosome and the listeners will be aware of that I!|m sure. The X chromosome is the !V the female chromosome and the Y is the male. So if you were a female you had two X chromosomes, it was highly likely that if you!|re a female, you would basically be a carrier. But males would be affected when they only had one X chromosome. So he, by screening all of those dogs with a test, he was able to identify the carriers and just by not breeding them there!|s no more Haemophilia-A that !V that we see any more in German Shepherds. There may be odd cases, I don!|t know, but we don!|t see it like we did in the 80s. And the thing about that disease, just before I finish !K transferred it back to a dog that was in Europe some years before and all his lineage had !V !¢FDcause he was a great German Shepherd had spread throughout the world.

SHANE HUNTINGTON
And I guess from the phenotype point of view, he looked !V

STEVEN HOLLOWAY
Beautiful.

SHANE HUNTINGTON
Beautiful !V but had a - a significant genetic problem that spread predominantly because of how great he looked.

STEVEN HOLLOWAY
And I guess some !V some diseases !V that one is a good example, is one gene. In other cases, there!|s many, many genes that come together and if you get a !V a high dose of those genes, then you!|re highly likely to develop the disease. And hip dysplasia!|s probably more like that, it!|s not a one gene effect.

SHANE HUNTINGTON
You!|re listening to Melbourne University Up Close. I!|m Dr Shane Huntington, and we!|re speaking with Dr Steve Holloway about canine DNA.
Steven now it!|s clear that with funding for obviously human diseases and human problems there is a lot of things being done there. We have a lot of hospitals, we have a lot of research institutes, and the like, but when it comes to !V to dogs, canines and !V and animals, I can imagine there isn!|t such a political pressure or such a !V a pressure coming from the general population to put large amounts of funding in this. How do you go about funding your work here in Australia?

STEVEN HOLLOWAY
There are some research grants that are available that are specifically veterinary. And, here in Melbourne we have one that!|s called the !V the Victorian Canine Research Foundation, and it!|s funded by dog breeders who pay their money into that and fund researchers like myself.

SHANE HUNTINGTON
So, this is a particular grant that!|s available to people within the state of Victoria, in Australia?

STEVEN HOLLOWAY
Yeah.

SHANE HUNTINGTON
And there!|s a group in Melbourne, we access that, specifically for this research. So we!|re not accessing some of the larger research schemes that are Australia-wide or !V or world-wide. This is specifically set up for dogs and - and this sort of work.

STEVEN HOLLOWAY
It is. Yeah, yeah, for diseases of dogs. And some veterinarians are funded by researching dog diseases that are good models for human diseases, by the main

human medical scientific research funds here in Australia. But that!|s an uncommon thing.

SHANE HUNTINGTON
Now in terms of support, I mean I have to say I!|ve never heard anyone ask people to get their dogs to give blood. As a clinician, do you find when you !V when you need blood to give to animals that come in, there is a shortage.

STEVEN HOLLOWAY
Well, the University of Melbourne has the canine blood bank and we have a dedicated team there at our campus at Werribee, which is out the western suburbs of Melbourne, and we supply blood and blood products such as plasma, etc.

SHANE HUNTINGTON
So I guess we should encourage people to get their dogs to give blood just as they do themselves and !V

STEVEN HOLLOWAY
And !V and anyone who!|s interested in doing that can contact us at the University of Melbourne. We have a !V a large number of greyhounds that are ex-racing greyhounds, and they!|re regular blood donors. Greyhounds are actually got a very high blood count and they!|re very, very amenable to giving blood. So, that provides probably about, I don!|t know, 70, 80% of our blood supply. But we also take donations from, generally, a larger breed dog.

SHANE HUNTINGTON
Something you can get a reasonable amount of blood from.

STEVEN HOLLOWAY
The Chihuahua!|s not going to be able to donate to a Great Dane if you know what I mean, so !V

SHANE HUNTINGTON
Now just !V getting back to the !V the dog genome for a moment. As we mentioned, there are similarities between, you know, aspects of !V of canines and humans. What sort of big things are on the horizon with regards to the outcome of the dog !V dog genome being sequenced in terms of potentially porting some of those ideas across to human treatments?

STEVEN HOLLOWAY
One of the things that we do is we!|ll closely look at what goes on in human cutting edge medical research. And often, if a !V a gene!|s found that predisposes to a certain disease in people, if that disease is seen by us in dogs as well, we go and look at the same gene in a dog, and we can find that gene now simply by using computer programs that localise the gene in the humans to its homologue in the dog. It!|s done on the web.

SHANE HUNTINGTON

Right.

STEVEN HOLLOWAY
Scientists use it all the time and - and cows and horses have been done as well now. So there!|s a large amount of comparative work. So, instead of having to go and do the exact same research from the ground up in dogs, we can see this is what happens in humans. Does the same thing happen in dogs? And a lot of times it does. And therefore, we can get more quickly to a diagnostic test and we can also use similar treatments that humans have available to them. On the other hand, if you were trying a new drug and there was a similar disease in dogs, you may want to see how it actually goes in dogs before you went and put it into people. That varies in some cases, the mouse is the model that !V or the rat, in other cases dogs are a !V a better model of the disease.

SHANE HUNTINGTON
And !V and is the information !V the genetic information that has been gleaned from !V from all this, is it been sort of funnelled out towards breeders, as you mentioned before with the German Shepherd to eliminate certain problems. Is that happening?

STEVEN HOLLOWAY
Absolutely. There is a company in Melbourne called GTG, a company that deals in human genetic testing and also canine genetic testing. You know, they provide services to look at different genetic diseases that breeders and veterinarians can actually access. And so there!|s eye diseases for example where there!|s a genetic test to test the parents to see if they!|re a carrier, and breeders do use those now. You!|d be surprised, they use a mouth swab. They just take a mouth swab from a dog and they can look at all the DNA and its use for parentage testing. For example, where there!|s sometimes [a] dispute over a Greyhound!|s parent. So it!|s widely used in the Greyhound industry now.

SHANE HUNTINGTON
Right. Dr Steve Holloway thanks for joining us today on Up Close and we wish you the very best of luck with your !V your research, and hope some great things come out of it in the future.

STEVEN HOLLOWAY
Well thanks very much for having me Shane.

SHANE HUNTINGTON
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