



# Playing with DNA

DNA testing is a modern miracle, but there can be negative effects to playing God with genes

There'll be no being mean to the KC this month (well not much, anyway). It's a time for celebration! And when you're counting your blessings, could I ask you to add something to your list? It's only a small thing - in fact, very small: DNA.

I'm worried now that you've all just turned the page. I didn't hear much excitement in *Dogs Today's* voice, either, when I told them what I'd be writing about this month, and I expect *DT's* amazing illustrator, Kevin Brockbank's, heart sank, too. But without the discovery of DNA, thousands more dogs would be suffering needlessly - from blindness, horrible neurological conditions, and a host of other debilitating, painful and sometimes deadly diseases. And that's because the discovery of DNA in 1953 has led - in the blink of an eye, really - to DNA tests that can help us avoid breeding dogs that will inflict these blighting problems on their puppies.

How extraordinary it is that the raw potential for everything about us and, of course, our dogs is encoded in something so small that until very recently even the most powerful microscope could not see it. And yet today we can send off a

drop of blood or a mouth swab from our beloved dogs and find out what's going on inside them at a level that would have been considered quite unthinkable just a few years ago.

Testing times  
Today, there are DNA tests for around 20 conditions in our dogs. Most are tests that can aim to give us an answer to: "Will this dog develop this condition?" Many more are on the way thanks to increasingly sophisticated technology that can identify genetic mutations faster than ever before. There's no doubt about it - DNA tests are a modern miracle.

Good breeders have embraced the concept of DNA tests with great gusto. Many have helped contribute financially and have donated blood/cheek swabs to researchers. And thanks to the current greater emphasis on health in pedigree dogs, there has been a many-fold increase in the number of breeders contacting the Animal Health Trust (the UK's main DNA-test development centre) to request and offer help in developing new DNA tests.

One of the most recent breakthroughs has been a new test for primary lens luxation (PLL), a painful, blinding

condition found in Miniature Bull Terriers and Lancashire Heelers. "Both breeds have been terrifically supportive and we absolutely couldn't have done the work without them," says the Animal Health Trust's Cathryn Mellersh. "They have volunteered DNA and information from their dogs and I have every confidence that they will use the test to its full advantage."

The PLL mutation is very common in Mini Bulls, so the chances of puppies being affected are very high. Now with this test, breeders can be sure that the puppies they produce will not go blind. Mini Bull breeders must be whooping with joy - and with good reason.

But something's been niggling me for a long time: a fear that we are relying far too much on DNA tests to bail us out of the trouble in which pedigree dogs find themselves, and that this gift from the geneticists is a double-edged sword.

The niggles turned to real concern at the publication of

a Kennel Club press release in July, entitled: "Eradication of inherited diseases in dogs moves a step closer". The opening paragraph went on to say: "The Kennel Club Charitable Trust strengthened its campaign to eliminate inherited diseases in dogs last week, as it signed its formal agreement with the Animal Health Trust (AHT), to jointly create the Kennel Club Genetics Centre and revealed some of the exciting findings so far."

Eradicate? Eliminate? Now, I'm all for optimism, but there are more than 500 genetic diseases in dogs (and twice that number according to some estimates) and we currently have DNA tests for fewer than 20 different disease conditions. The KC press release went on to say that the AHT will be looking to develop a further 25 tests in the next five years - all welcome, but still only a handful in the greater scheme of things.

In fact, any talk of elimination of inherited disease in dogs is not just hopelessly premature - it's dishonest. There isn't a hope in hell of eradication and why anyone sanctioned the KC press release's headline is beyond me. Genetic disease is a fact of life (ironically, a statement often used by those defending what they see as the 'attack' on pedigree dogs). Really, the most we can hope for is to reduce problems to an acceptable level, and DNA testing, while a wonderful tool, will only ever be part of the answer.

Easy fix?  
In the past few years, the Kennel Club has set great store by DNA tests, hence its considerable funding for the Animal Health Trust. And you can understand the appeal. Quite simply, DNA tests appeared to offer the hope that you can fix problems without changing, fundamentally, the way we breed dogs. In other words, that we could continue to inbreed dogs to achieve the specific look/traits we want without paying the price in doubling up on the genetic

disease that also tends to spread with inbreeding.

But there are problems. First up is that the ability to look deep into our dogs' DNA has revealed much more than dodgy mutations; it has shown us the nuts and bolts of what we've done to the dog genome - which is, essentially, to knacker it through inbreeding in the pursuit of certain traits that often have little to do with health. There is a price to be paid for this, as it is increasingly obvious that inbreeding impairs our dogs' immune systems, making them increasingly vulnerable to infection, allergies and other immune-mediated problems, even cancer. In fact, a group of Italian researchers has just found that purebred dogs are twice as likely to suffer from cancer as their random-bred cousins. A shocking statistic.

Second, all the current DNA tests are for conditions that are, in a genetic sense, simple. Most are caused by single mutations that are pretty easy for the gene hunters to spot. But lots of problems in dogs are much more complicated than this. We know, for instance, that there are likely to be many genes involved in hip dysplasia and that diet and exercise play an additional role in whether or not a dog is affected clinically.

Three years ago, when I spoke to the KC's genetics advisor, Jeff Sampson, about this, he was confident that there would be useful DNA tests for complex disorders like hip dysplasia. But today the emphasis is shifting towards developing estimated breeding values (EBVs) for complex disorders like hip dysplasia. This, essentially, is a breeding tool that assesses risk using nifty computer programmes into which can be fed all kinds of different information about a breed - population size, the level of inbreeding, health-test results and so on. All breeders need to do is type in the names of the two dogs they wish to mate and out will pop an EBV score, which will reveal if it's a match made in health-heaven, or health-hell.

The beauty of EBVs is that they should be reliably predictive independent of DNA tests, although DNA data can be incorporated if and when it becomes available. The hope is that EBVs will be better than what we currently have for complex disorders. In the case of hip dysplasia, for instance, the early evidence is that EBVs are better at predicting an offspring's hip scores than the hip scores of the parents, which is how we tend to do it at the moment.

Holistic view  
I like the idea of EBVs because they have the potential to look at the whole dog in the context of the whole breed. I think we need to think more holistically about genes, too. Because although we talk merrily about the gene for this and for that, genes are not discrete entities that just do one thing. Genes can and do play many roles - both individually and in combination with other genes. And neither are they pantomime goodies or baddies.

"It is risky to focus on just one gene at a time," says biologist and Saluki breeder John Burchard. "The idea that there are 'bad' genes and 'good' genes and that you can eliminate the 'bad' ones while keeping the 'good' ones is at best a dangerous oversimplification. Genes do not exist, or act, by themselves."

The classic example of this is the genetic mutation that predisposes Africans to sickle-cell anaemia. It turns out that this mutation is life-saving in another respect: it protects against malaria. So this mutation is both good and bad. Now we don't go much for genetic engineering in humans - but if we had decided to try to breed it out, millions more would die of malaria. We need, therefore, to be very careful about playing God with genes.

This is particularly true with DNA tests for what are known as 'heightened-risk' genes. While some DNA tests are pretty conclusive - ie if the dog has the mutation (or a double-dose if it's a recessive condition), they will





almost certainly develop the disease. But others are not definitive. Boxer breeder and geneticist Bruce Cattanach is currently struggling with the new 'heightened-risk' DNA test for degenerative myelopathy (DM) in Boxers. "The test will tell you which dogs have two copies of the mutation and are theoretically likely to develop DM," says Bruce. "The problem is that although British-bred Boxers have tested positive for the mutation, we have no reports of DM in Boxers in the UK."

#### A tough choice

The problem may be because DM is a late-onset condition. Perhaps Boxers are simply not living long enough to develop it? Or perhaps, as is very likely, other genes yet to be identified are exerting an influence? So do breeders simply remove otherwise good dogs from the gene pool when it's by no means certain they would develop the problem? It's a very tough choice.

"It's also exceedingly unlikely that this gene does nothing else other than affect the probability of DM," adds Saluki breeder John Burchard. "One of the things it almost certainly does is form part of the 'environment' in which other genes function. If you start tampering with that, the law of unintended consequences is all too likely to rise up and bite you in the backside. That's the danger of overenthusiastic DNA testing - most of the time we are indeed still tinkering in the dark."

That said, it's clear that some mutations do much more

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harm than good and we'd be well shot of them. We need to do it carefully, though, and over several monitored generations to be sure we're not losing something important. It's for this reason that witch-hunts against dogs who are just carriers of a particular condition (but not themselves affected) are misplaced. There is no reason why these dogs cannot be bred from, as long as it's to a 'clear', as none of the puppies will be affected. Some may themselves be carriers, but as long as they are themselves DNA-tested and bred carefully, there is no risk. In this way, we will not further impoverish the small gene pools that threaten some breeds.

Finally, there's the issue of cost. DNA tests through the Animal Health Trust currently cost about £50 each. As more tests come on-stream, DNA testing could become prohibitively expensive for breeders of some breeds.

"If I want to know if an adult Borzoi has cardiac problems, the least expensive way to do it is to take him to a lure course and test run him on an 800-yard course," says Bonnie Dalzell, a US breeder of wonderfully fit and functional working Borzoi. "If he can do that at full racing speed twice in a row, his heart

is probably okay. Currently, there are so many different ways that cardiac problems can be caused that the idea of having genetic testing for all of them is very difficult and could add up to thousands of dollars."

The AHT's Cathryn Mellersh predicts that breeders will one day be able to submit a single sample that will be run against all the known problems at a much cheaper cost than doing them all individually. She also points out that knowing that your dog, for instance, will not develop a blinding eye problem may negate the need for expensive annual eye tests.

#### No guarantee

But a reality check is still in order. DNA tests are a wonderful resource - truly. But they are in themselves no guarantee that a dog is healthy because they measure just a tiny part of the whole dog. They are also no excuse for not tackling the fundamental reasons why genetic disease has become so prevalent in some breeds of dog - essentially a kennel-club system that, to date, has promoted inbreeding and placed too much emphasis on how a dog looks. But that, we hope, is changing... ■

Jemima Harrison is a journalist/TV producer best known for making *Pedigree Dogs Exposed*, the BBC1 film that highlighted health and welfare problems in pedigree dogs. Jemima owns a working Flat Coated Retriever and several crossbreeds. Passionate about dogs, she also runs a small independent rescue specialising in finding homes for retriever crosses

