

Do These Genes Fit?

I heard about the PRA research for Aussies. My dog is clear as of last CERF, but I know he has close relatives who aren't. The owners of those dogs won't participate in the study. One of them called it a "witch hunt." Because of this, I don't even have a shot at determining if my dog is a carrier prior to breeding him. Is there anything I can do?

Fortunately, their ostrich tactics will not affect your need to know your dog's Progressive Retinal Atrophy status. There is already a DNA test on the market. Aussies have been found to have the progressive rod-cone degeneration (prcd) form of PRA. It is the most common PRA in dogs, though rare in Aussies. The test was developed a few years ago following research on other breeds.

You can screen your dog and know exactly what his status is before you breed. In the US, the test is available from OptiGen: www.optigen.com; 607 257-0301.

This one was easy for us because there has been a lot of research on PRA in other breeds. A number of genes have been identified and DNA tests developed. PRA is always single-gene and usually recessive, but it can be caused by different genes. When an affected Aussie was presented to Optigen, they checked its DNA for the previously identified genes and hit the jackpot.

Fortunately, PRA is very rare in Aussies. If you have other dogs, it will not be necessary to screen them unless they are within two steps of relation to a dog that is affected or has been identified as having at least one copy of the prcdPRA mutation through DNA testing.

I know you have always questioned the validity of "dominant with incomplete penetrance". Do you feel the mode of inheritance for cataracts will be the first documented case of "incomplete penetrance"?

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I have questioned it as a proposed single-gene mode of inheritance. When traits appear to be dominant with incomplete penetrance it most probably means that there are other genes that influence the phenotype so sometimes you see it and sometimes you do not. My biggest objection to the terminology is that it is too often used as quasi-scientific excuse for finger-pointing between stud and bitch owners: Who is responsible for passing the gene is of course dependent on which one the person owns!

In the case of the cataract mutation recently identified, it may be dominant with incomplete penetrance because all affected dogs in the study have at least one copy of the mutation. (All dogs with two copies have cataracts.) Some dogs with only one copy do not have cataracts, but at this point they don't know if that is because the dogs won't ever have them or because they don't have them yet.

Cataracts in Aussies definitely have something called "variable expressivity." They can start in young dogs or not until a dog is eight or older. The speed at which the cataracts progress varies from rapid to so slow the dog has functional vision all its life. Given the occasional late onset of this disease, the clear dogs in the study that have the mutation still might develop cataracts later in life.

If some of the non-affected dogs that carry this mutation live on to old age without ever developing cataracts, then this may be the first well-documented case of a variable with incomplete penetrance trait in dogs. But it still isn't single-gene because other genes, which may come from either parent, and possibly environmental factors,

would be the root cause of the variable penetrance.

Someone told me that if a dog has a low COI that means risk for epilepsy is low. Is that correct?

Absolutely not. The coefficient of inbreeding (COI) is *only* a measure of the level of inbreeding a particular dog or cross might have. It is not, all by itself, a predictor for any specific trait. However, the closer the breeding and, therefore, the higher the COI, the more likely you are to produce traits known to occur in that line—any traits, good *or* bad. After all, that is the reason people linebreed—in hopes of concentrating genes for the traits they want to perpetuate.

But there is also a dark side to close breedings. If a line is known to have a problem with epilepsy, or any other unwanted trait, and you do a tight breeding with dogs from that line, you will increase the COI and will probably increase the epilepsy risk because the trait is known to occur in that line. On the other hand, if you did a breeding with 0% COI—say a Poodle to a Cocker Spaniel—you could have very high risk for epilepsy if both parents had previously produced it.

For a fuller explanation of what COIs are and how you can put them to use in a breeding program, read this article: http://www.ashgi.org/articles/breeding_coi.htm.

I heard that hemolytic anemia isn't inherited after all. It's something your dog can catch from other dogs. True?

Mycoplasma haemocanis, the organism that can cause immune-mediated hemolytic anemia, is transmitted by ticks. Therefore, it can't be passed directly from dog to dog. But not every dog infected with *Mycoplasma* gets IMHA, nor is it the root cause of every case of IMHA. The disease can be inherited and it may also be secondary to another autoimmune disease.

IMHA is one of the autoimmune diseases I get reports of fairly frequently. Some of the cases show a familial pattern, so it is extremely likely that we have an inherited form. In the case of secondary IMHA, the primary disease may also be inherited. The form associated with *Mycoplasma* probably is not.

Assuming every case of IMHA is due to *Mycoplasma*, and therefore not inherited, could further the spread of a nasty and potentially lethal inherited disease. However, failure to recognize those cases that are caused by a *Mycoplasma* infection could result in the dog not receiving the proper treatment. That could be lethal to the dog.

As a breeder, how can I best use the MDR1 test? Will I have to keep testing dogs forever?

The test is a direct gene DNA test, so you will know the genotype for each dog from its test results. If the parents are both normal/normal (they use +/+ in Europe) then they can't pass the mutation to their pups, so the pups wouldn't need testing.

In such a case you should give your puppy buyers a copy of the parents' reports for their records. That way they won't wind up testing the dog unnecessarily and can show their veterinarians the dog is not at risk for MDR1 reactions. Breeders who buy a pup will then know the pup's genotype when they make breeding decisions.

As time goes on and more dogs are screened, you could determine the need for screening any particular dog by checking the pedigree for known test results. If you find normal/normal ancestors along every line of descent, there's no need to test. But if even one line is unknown or has a dog with at least one copy of the mutation, you will need to do so.

The MDR1 test was recently added as an optional CHIC requirement for Aussies. Check OFA's Web site for information on how to submit your results.

If you breed a long-backed dog with a short-backed bitch, wouldn't you get long and short rather regular? I would think you should breed a long with a normal to get the better. If I understand it,

genes don't intermingle with each other, offspring get one or the other.

Aspects of conformation that involve skeletal structure are not single-gene traits, so inheritance is not simple or easy to predict. Generally speaking, if the parents are of opposite extremes the pups could fall anywhere on a continuum between the two parental types and may or may not be consistent among themselves depending on what specific genes the parents each have and how they fall together in the pups.

Any time a dog is off the ideal for a conformation trait, but not so far off that it shouldn't be bred at all, the best plan is to select mates that are near perfect in that respect and come from families where correctness of that trait is the norm.

If back length is inconsistent in the prospective mate's extended family or, worse, it is one of the few in that family that has correct length of back, you probably won't get the improvement you are looking for in the litter.

Genes don't "intermingle" but they can interact. Some are simple dominant/recessive (like black/red color.) With other genes, both copies may contribute something to the phenotype (what you see or can measure.) Many work in concert with a number of other genes to produce a particular phenotype and with these polygenic traits the potential results can fall anywhere within a given range (i.e., long back to short back) with most individuals in a given breed falling closer to the middle than to either extreme. However, in a single litter, the results are unlikely to form this sort of "bell curve" distribution because there are relatively few individuals in even the largest litters of pups.

My cousin has a "Labradoodle." She and I are having a friendly argument about genetic health of purebreds versus mutts. She says purebreds have higher levels of genetic disease. I did a little research and I think that mix-breeds have way more kinds of genetic problems than any purebred. So who's right?

You both are.

Mix-breeds, as a class, have more inherited diseases than any single pure breed because of their broader gene pool. However, the frequency of any given disease is likely to be lower, again because the population is more diverse. Yes, you can

Featured Research*

Project: Genetics of Impulsive Aggression in the Dog

Goal: To locate genes involved in anxiety-based impulsive aggression and fear aggression in canines. Current focus: Impulsive Aggression.

Conducted by: Steve Hamilton, MD, PhD
University of California, San Francisco
Karen Overall, DVM
University of Pennsylvania

Samples needed from:

1. Australian Shepherds with this type of inappropriate aggression that exhibit abnormal, aggressive behaviors grossly out of proportion or out of context with the external environment.
2. Unaffected relatives of dogs who exhibit this behavior.
3. Large families containing dogs who are both affected and unaffected.

Sample type: Cheek swabs or blood samples.

Pedigree information greatly appreciated if available.

All information submitted to this project is confidential.

Contact: Jennifer Yokoyama, Graduate Student
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*See next page for more information.

find inbred mutts, but we are talking about all mix-breeds together.

The increased frequency of specific genetic issues in specific purebreds, over that of the species as a whole, is what makes them good study subjects now that the genome is complete. Since that was accomplished, research into canine genetic diseases has markedly increased.

Some diseases, like epilepsy, are very common in mix-breeds as well as purebreds, however, there are many genetically distinct forms of epilepsy. It isn't really "one" disease from a genetic standpoint, though clinically it is still treated as such. That situation may change as science discovers exactly what is going wrong in different forms of the disease and devises treatments tailored to each type. In the case of this particular disease, the mutts have many epilepsies, while individual pure breeds will have one or possibly a very few types.

Thyroiditis is another disease frequently diagnosed in mix-breeds as well as purebreds, but I think there is a good argument to be made that it is also an over-diagnosed disease. So are we actually seeing high numbers of affected dogs or does our method of diagnosis need refinement? The jury is still out.

"Designer" dogs like your cousin's Labradoodle and the ubiquitous whatever-a-poos are not really in the same class as mix-breeds because they have been purposely bred from dogs of specific types or breeds. Not all are truly hybrid because there are people who are going beyond the F1 (first) generation when breeding them. You likely will see higher incidences of some diseases in those F2 and beyond dogs, dependant upon what the founder stock was. For instance, if the parent strains or breeds had HD, you might be OK in the F1 but once you got to F2 or started back-crossing to either parent strain, it will be there again.

Genetics of Impulsive Aggression in the Dog A New Research Project

We are genetic researchers from the University of California, San Francisco. We are working on the Canine Behavioral Genetics Project, investigating the genetics underlying various anxiety-related behaviors such as noise phobia, separation anxiety, fear aggression, and impulse control problems. As members of the Department of Psychiatry, our hope is to identify genetic markers that may predispose dogs to certain behavioral traits, with future goals of applying this knowledge to better treatment of affected dogs as well as learning more about related pathways in human disorders.

One of our projects involves studying aggression, a complex behavior that is probably influenced by a combination of genetic and environmental factors. We work under the assumption that many aggressive behaviors are related to underlying anxiety conditions. Specifically, we are interested in maladaptive, anxiety-based fear-aggression, and impulse control aggression. Dogs with this type of inappropriate aggression exhibit abnormal, aggressive behaviors that are grossly out of proportion or out of context with the external environment. We are very interested in the genetics and biology behind this trait.

We realize that this is a very controversial trait to research and want to assure you that our entire group has publicly criticized breed-specific legislation. It is clear that this type of inappropriate aggression is seen throughout all breeds of dogs. It is our hope that by identifying genetic markers for predisposition to this type of aggression, we might better address the need for modified training practices at a young age and improved breeding and puppy-raising practices, which we hope will remove the negative stigma associated with particular breeds.

The dog provides a unique opportunity to study the genetics underlying different behaviors. Because dogs from the same breed are more genetically similar than dogs from different breeds, studying single-breed groups makes it easier to find genetic markers that may predispose certain dogs to behavioral traits. Discoveries made in one particular breed can then be extended to other, closely related breeds for confirmation of findings (e.g., Australian Shepherds vs. Collies). Given the strong interest in genetics within the Australian Shepherd community, we have sought to initiate these studies with a breed where the importance of genetics for understanding the breed is well-established.

It is our hope that we can find a way to garner support for this project in a positive light, making clear the benefits for the scientific and dog communities while ensuring **complete confidentiality** for owners and their dogs.

We are looking for Australian Shepherds affected by this inappropriate form of anxiety-based aggression, their unaffected relatives, and large families containing dogs that are both affected and unaffected. If pedigrees are not available, we are also collecting unrelated single cases with these behaviors. If you are interested in participating or have any questions regarding our project, please feel free to contact Jennifer Yokoyama at the email address or phone number below. You can learn more about our studies at our Web site: <http://psych.ucsf.edu/K9BehavioralGenetics/>.

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