

Dog Health Workshop, Dortmund February 14. -15. 2015

Notes from Workshop 3, Genetic testing

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Topics for discussion, based on a brainstorming in the group

- DNA bio banking
- Validation of test
 - Breed
 - Population
 - Frequency of the disease allele
 - Quality control – Dog ID
 - Nature of mutation, for instance copy number variation
 - Mode of inheritance
 - Penetrance
 - Complex diseases
 - Genotype/phenotype correlation
- Laboratories
 - Accreditation
 - Intellectual Property Rights
 - WGS and multiplexing
- Genetic counseling
 - Whose role?
 - Veterinarians (practitioners)
 - Breed clubs/Kennel Clubs
 - Diagnostic tool – prevention/control
 - Costs – accessibility
- Standards for parentage tests
 - Of test modality

DNA Bio banking

Many researchers and organizations have collections of dog DNA with or without disease phenotype information. It would be beneficial if the IPFD could create a registry of stored DNA samples with location, numbers, and disease phenotypes which can then be use in a collaborative fashion between researchers

Release forms for DNA Banks should contain a check off that allows for sharing with other researchers or projects

Validation of DNA test

Peer-reviewed publication is preferred, although not always possible. If a test is not patented, publication allows any commercial lab to start offering the test. The result is loss of research lab testing revenue to cover development costs and refine epidemiological questions.

A system can be developed where test validation can be graded based on whether it has undergone peer review, been submitted, or has not been submitted for peer review.

Questions to be answered as part of an evaluation:

- Is the test based on a causative or risk-associated mutation?
- Is the test valid and correlated to the disease in:
 - The same breed in other countries/populations?
 - Other breeds?
- The IPFD should evaluate some form of test validation

The group could not determine factors which would dictate whether a genetic test should be offered to/utilized by an entire breed. There are too many variables including severity of disease, frequency of mutation in the population, population dynamics, etc.

Identification of the dog being tested is crucial. Testing labs should identify on the test result certificate whether verification of identity (microchip) was validated by a veterinarian. If dog identification is not validated, the “clear by parentage” designation should not be offered by registries.

The labs should include information about the nature of the mutation. Is it a direct test for a causative mutation? Generally, there is a lack of functional studies for many tests. Is the test for a known liability gene for a complex disorder or just for a genetic marker linked to liability in a finite population? Copy number variations are very unstable and the number of copies can increase with each generation.

The use of multiplexing of genetic tests to be run on every breed is problematic, as most mutations have not been correlated to disease in every breed. This is an issue with mutations related to complexly inherited disorders. The future utilization of whole genome sequencing (WGS) of individual dogs will also make this an important area of discussion.

Validation of labs

There should be some minimum standards for laboratory quality control including general laboratory standards and prerequisites for a lab to run a new test. The IPFD can work with representatives from testing labs to set standards.

Intellectual property rights: If a lab holds patents and licensing rights on a test, they should be honored by other labs, and registries. Legal aspects of patents and breeding recommendations will have to evolve with the times. In Sweden, it is illegal to mate a DNA tested carrier with a dog of unknown status. This is problematic for several reasons; multiplexing tests and tests for risk factors.

If multiplexing or whole genome sequencing in a commercial setting identifies mutations not known to occur in the breed, the testing lab should investigate and validate the results as they correlate to disease phenotype in the breed (preferably prior to informing the owner).

Genetic counseling

Laboratories have a responsibility to provide basic genetic counseling. This includes information to the owner regarding the nature of the genetic test, what the results mean and links to resources where they can go for further information. Breed clubs and National kennel clubs also have a responsibility to breeders and owners regarding applicability of genetic tests and genetic counseling.

Genetic counseling recommendations will vary based on the mode of inheritance of the disorder, frequency of the mutation in breed populations (which can vary within breed varieties, as well as between countries), penetrance of phenotypic expression, severity of the disease phenotype, and breed pool size and diversity.

Veterinary education lags behind regarding the understanding of genetic disease testing and genetic counseling. WSAVA has a role to recommend more in depth veterinarian education.

Parentage testing

It would be beneficial to have a DNA fingerprint on tested samples to validate identification and parentage. However, this would increase the cost of tests. DNA identification has not been standardized but ISAG is working on standardizing dog DNA identification.