# ANKC'S DNA TESTING PROGRAM

## Executive Summary

ANKC's DNA program is ready for commencement as planned on January 1, 2006. This is a soundly based program with major potential and a great deal of diligence and hard work has been put into getting it to this stage. We can look forward to achieving significant results with it as it gains momentum.

Following the decision in May to defer compulsory profiling/parentage testing of breeding stock, the immediate focus of the program will be with the Breed Councils/Clubs, especially with those breeds where there are genetic tests available for hereditary diseases. There are significant benefits in disease prevention within these breeds, as well as financial benefits to breeders and owners from adoption of the program, ie.: -

- pedigree assurance via profiling and parentage testing
- lower cost genetic disease testing
- accurate disease clearance via parentage testing where both parents have clear disease status, with significant savings compared to ongoing disease testing
- Stud Book Registration for complying breeds, providing a sound basis for advertising and promotion.

This report also covers items requested by ANKC in minutes of its May 2005 meeting.

ANKC's DNA program has much to offer in the short term, especially in accelerating the genetic testing and reduction of hereditary diseases. Its long term potential remains and should be demonstrated by success once the program commences.

Representatives of Genetic Technologies Limited (GTG) and myself are available to meet with Member Bodies, breed councils and clubs to discuss and resolve any issues relevant to the program and its commencement.

Bob Maver
Canine Health Committee
August 12, 2005

# ANKC'S DNA TESTING PROGRAM

## Introduction

The ANKC program focuses on breeding stock with the long-term objective that every dog and bitch on a pedigree will have parentage verification. It is also unique in combining genetic testing for hereditary diseases, providing synergy and significant benefits in disease prevention and cost reduction in disease testing. Integration of profiling and disease testing provides accuracy and cost minimisation. Features of the program include: -

- positive identification of dogs presenting for test
- independent, trained sample collectors
- use of superior, "gold standard" technology for profiling/parentage testing
- advantageous pricing
- accurate disease testing over a range of genetic disease tests
- fast results
- professional genetic advice
- retained DNA samples for future tests if needed
- accurate disease clearance via profiling where parents are clear
- all profiles and disease tests on the one database for cross reference
- full customer service.

Protocols have been established and tested for achieving efficient procedures and accurate results. GTG has verified and released a number of DNA-based disease tests and is building the ANKC database for parentage testing across all breeds, in preparation for commencement of the program. The program is based on logic, common sense and the use of science to achieve results. It will work if we give it the support it deserves. Key components of the program include the service provider and database development.

## DNA Profiling, Parentage Testing and Pedigree Assurance

In any purebred species the cornerstone is the pedigree. It is meant to be a true record of the ancestors, and accordingly is a vital factor in breeding programs. Over many years there have been instances of canine parentage error and pedigree falsification, but with the advent of DNA profiling it has been found that a 10% parentage error is typical of purebred populations across different species and even much higher in some.

The shock for the dog world was the result of a major DNA parentage survey by the American Kennel Club (AKC) and the realisation that the 10% error can apply to purebred dogs. The AKC survey cost the organisation over $US 500,000. AKC responded by introducing compulsory testing for frequently used stud dogs, covering approximately 40% of all litters. The result has been an immediate reduction in parentage error to less than 5% in that sector of the register, as fraudulent pedigree activities would be automatically eliminated and, probably, breeders began to take better care of bitches in season when mated to frequently used sires. The remaining parentage errors (less than 5%) were largely due to second/unknown matings of the same breed. Correction of those remaining parentage errors has been possible in most instances by checking back on other dogs on the premises at the time. Only a few parentage errors were from crossbreed matings. To illustrate the position, in the month of October 2004, AKC cancelled 88 litters for parentage error and 4 for impure breeding, but was able to register 78 corrected litters. Crossbreds are usually readily identifiable as each breed has certain common DNA characteristics.

It is worth noting also that the first objective expressed in the AKC's Mission Statement is "Maintain a register for purebred dogs and preserve its integrity".

We can question whether the 10% applies to ANKC registered dogs, but why would it not? Should we conduct a survey here or just get on with the job? ANKC does not have the money for a significant survey, but the Australian picture will become clear as the ANKC program progresses.

Implications of parentage errors are serious - with a 10% parentage error in each generation: -

- 10% of dogs have half their pedigree wrong, or of 1000 dogs at a show, 100 would be likely to have the wrong sire
- the average 4-generation pedigree would have close to 20% error in terms of genes present.

Large scale pedigree errors are intolerable in breeding stock of any purebred register.

The good news is that while DNA testing does not of itself reduce the error it does allow correction in most cases as shown by the AKC experience.

**Position of Other Purebred Animal Organisations**

Worldwide, given the errors identified by DNA profiling, major purebred animal associations have already introduced DNA programs to improve accuracy in their registers. A survey showed the main Australian breed associations for horses and cattle together with Greyhounds Australasia all have compulsory DNA profiling schemes for that reason. Various overseas canine bodies now have DNA programs, including AKC (compulsory) and the Kennel Club UK (voluntary). DNA profiling is becoming standard for proof of identity in import/export of dogs and for frozen semen donors.

**ANKC's Position**

As the registrar of purebred dogs in Australia, ANKC has a fundamental responsibility to make all reasonable efforts to ensure accuracy of the breeding stock register (ANKC's lawyers Barnes & Wenden, May 2005). ANKC's DNA program has the potential to eventually provide this, however a voluntary program does not address: -

(a) fraudulent pedigrees resulting from types of activities which are known to occur, including
- sire substitution, to reduce overuse of popular sires (eg. the Tony Lackett case in Greyhounds)
- "topping up" litters by additional mating with a second, prolific sire to increase the numbers within a litter
- phantom bitches, whereby a bitch may be mated each season and every second litter registered to a phantom bitch, anecdotal evidence indicates this is a common practice in small dogs which have small litters
- substitution of puppies from other litters where demand exceeds supply for a particular litter (eg. GSD case, refer VCA's former Field Officer, R. Jensen)
- substitution of puppies from unregistered litters (eg. Rottweiler case, refer VCA's former Field Officer, R. Jensen).

(b) parentage across the broad register of breeding stock, as obviously the DNA profiles of both parents must be on the register for parentage of offspring to be verified.

Expeience of the Kennel Club (UK) is that few breeders bother to participate in its voluntary parentage program, with approximately only 4000 dogs having DNA profiles recorded in a 5 year period, or less than half a percent! Clearly this does not provide a significant effect on integrity of the register. The long-term objective of mandatory parentage for breeding stock should eventually happen, as the benefits become obvious.

However the option is available within the ANKC's Litter Registration Limitations program for Breed Councils/Clubs to require parentage checking. Various Breed Councils are viewing this favourably, particularly where there is a genetic test available for a disease that is a problem in the breed, as discussed below.

There must be one operational database for DNA profiling and parentage testing for the program to operate efficiently. GTG was selected to perform these functions using the "gold standard" MMI markers for a number of reasons(see Page 8).

Note: Just prior to the May meeting of ANKC some seriously flawed and misleading information was distributed in relation to the MMI markers as used by GTG for DNA profiling and parentage testing. Suffice to say that AKC and MMI were incensed by such comments and have advised that these markers have been 100% effective in use with over 400,000 results on record.

**Genetic Testing for Disease**

Whatever the mode of inheritance of the disease, once there is a direct genetic test available then that disease can be prevented from further occurrence by determination of the genetic status of breeding stock and use of an appropriate selection program. ANKC must do all it can to promote disease prevention, for the benefit and protection of the dogs, puppy buyers and breeders.

There are around 350 hereditary diseases when added across the various breeds. Currently tests are listed for more than 50 of those, mostly patented by various overseas organisations. Since publishing of the canine genome in 2004, research into new tests has accelerated and we are already seeing tests released at a faster rate and at lower cost.

DNA testing is a powerful tool in disease prevention, but it must be used sensibly for accuracy and to minimise costs to the breeders. We already have examples of success in Australia and the opportunity for disease prevention is expanding rapidly as research locates the disease-causing genes.

Responsible breeders must use every reasonable means of prevention of hereditary diseases. However use of DNA tests has been inhibited by relatively high costs of overseas testing and the need to test each generation. Accordingly few breed programs

have resulted. A major advantage of the ANKC's DNA program is that, where there is a DNA direct (not linkage-based) disease test, it allows prevention of that disease in just one generation, and without culling of current breeding stock in the main. Where both parents have their genetic status determined for the disease according to ANKC protocols (positive identification and independent DNA sample collection to ensure accuracy) then matings which could produce affected puppies may be avoided. A unique feature of the program is that in the most common cases where the disease has an autosomal recessive mode of inheritance (eg. PRA, vWD, NCL), if both parents have clear status then offspring can be cleared by the low cost parentage test, generation after generation. Also, with autosomal recessives, the causative gene may be eliminated in one generation, or more depending on incidence in the breed, and with minimal effect on the gene pool.

GTG offers an expanding range of genetic disease tests at lower costs, but owners may use any recognised laboratory for disease tests, but recognition under the ANKC program requires compliance with ANKC protocols for collection.

The DNA program should provide a stimulus for wider use of DNA-based disease tests and resulting disease prevention. DNA technology provides the tool - the program will do the rest.

**Stud Book Registration**

The concept of a Stud Book is well recognised in the community. The idea of including Stud Book Registration as a component of ANKC's DNA program is to establish a higher classification for those breeding stock which comply with criteria directed at producing better offspring.

It is proposed that the criteria are to be: -

- DNA profiled according to ANKC protocols
- parentage proven by DNA test according to ANKC protocols ( except for current breeding stock for which parentage is accepted as the starting point)
- compliance with any Litter Registration Limitations in place for parents within the breed.

Stud Book Registration has the potential to improve future offspring by ensuring that breeding stock meet requirements laid down by the Breed Council/Clubs together with ANKC. This special status of DNA profiling/parentage/disease testing will provide a

sound and credible basis for breed promotion and breeder advertising, resulting in higher demand and price for puppies.

There may be a cost applied by the Member Body for issue of a certificate for Stud Book Registration..

**Summary of Benefits of the ANKC's DNA Program**

Where the program is utilised there is potential for the following benefits: -

**1. Benefits to The Dogs**

The prime consideration is prevention of disease, achievable through greater acceptance of genetic testing through

- lower costs of local disease testing
- pedigree clearance for disease.

**2. Benefits to Puppy Buyers**

- guarantees of freedom from specific diseases when recommended breeding programs are in place according to the mode of inheritance of the disease
- a degree of quality assurance afforded by Stud Book Registration in terms of pedigree and disease status.

**3. Benefits To Breeders (see Appendix for cost/benefits)**

The program provides: -

- certainty that breeding stock and their pedigrees are as purported - fundamental to breeding plans
- opportunity to promote their kennels and stock through having breeding stock Stud Book registered, justifiably raising status compared to unregistered pedigreed stock and crossbreds
- facility for profiling of dogs and frozen semen for export where required
- added impetus to exports of Australian stock as the importance of pedigree assurance, genetic disease status and Stud Book registration become fully appreciated
- prompt and accurate parentage testing and advice for breeders in cases of doubtful parentage of litters
- where there is a test for a genetic disease test, prevention of the disease in one generation without culling current breeding stock in most cases
- accuracy in genetic disease clearance of offspring from clear parents simply by parentage testing, so avoiding the higher cost disease tests

- the one DNA sample may be used for profiling and disease tests and stored without fee for any future tests
- access to a range of additional disease tests through GTG's cross-licensing via its patent strength
- protection from litigation relating to disease affected puppies
- international compatibility of DNA profiles for export/import of dogs and semen due to GTG's ability to use the superior MMI markers and also those of ISAG
- GTG's,low pricing, accurate results and full customer service.

**4. Benefits To ANKC**

Where the program is utilised it provides : -

- pedigree assurance so that pedigrees of breeding stock eventually become completely accurate (where there is mandatory participation)
- reduction of hereditary diseases
- the program protects the ANKC and Member Bodies from litigation in relation to accuracy of breeding stock pedigrees and hereditary diseases
- improved public credibility as indicated by enthusiastic acceptance received on announcement of the program from responsible breeders, breed councils, the general media and the AVA (even though it will cut across incomes in the profession)
- opportunity for the ANKC to raise the public image of pure bred dogs on the basis of responsible breeding and predictability
- simplified administration of eligibility for breeding, as those meeting requirements will be on the Stud Book Register
- Member Bodies are able to cover costs involved
- Member Bodies have the opportunity to generate profits from services provided in sample collection and data processing where desired.

**<u>GTG and Development of the Program</u>**

GTG was originally selected as service provider because it was: -

- the only DNA laboratory prepared to do both parentage testing and provide a range of genetic disease tests at a significantly lower pricing structure than others
- the only Australian DNA laboratory able to use both MMI markers, for DNA profiles compatible with AKC (by far the biggest canine database in the world), and ISAG markers used in various smaller databases



- prepared to provide full customer service (education, program promotion, low cost collection, sample processing, testing, certificate issue, personal contact and advice)

- flexible in working with Member Bodies and Clubs to give discounts for those organisations to generate income from performing DNA sample collection, processing and recording within the framework of the program
- prepared to develop the operational database and down load details to ANKC as required
- experienced in DNA sample collection across a broad range - human paternity and forensic cases and across many animal species.

GTG has been extremely active in developing the program by : -

- developing, proving and introducing a range of genetic disease tests
- developing appropriate protocols and proving their performance
- obtaining rights to the superior MMI genetic markers, as used by AKC, becoming the only laboratory in Australia able to offer compatibility with both MMI and ISAG profiles internationally (note ISAG does not have a commercial marker set available as yet)
- developing the database for parentage and genetic disease test results for down-loading to ANKC when required
- establishing the range of marker alleles across each of the breeds for breed characterisation, with hundreds of profiles done at GTG's cost
- promotional visits to shows around Australia, educational talks at clubs and meetings
- direct contact with owners and breeders
- conducting research into a number of genetic diseases
- assisting breeders by conducting parentage tests and disease tests and offering advice where requested.

**Database development**

GTG has developed a computer program to handle the operational database for profiling parentage and disease test results and is compiling these results for down-loading to ANKC on a regular basis as required. It is extremely important that ANKC develops its computer capability to accept the data generated, preferably linked to the pedigree register so that analysis of hereditary disease results for parents, offspring and siblings is possible as a resource in disease prevention.

**Protocols**

Copies of the protocols document have been provided to Member Bodies for consideration at ANKC's October 2005 meeting. Note copies of the protocols document were supplied to ANKC in January 2005 and distributed for consideration by the Canine Health Committee. The intention was for the protocols to go forward to ANKC with the agenda documents for the May 2005 meeting, attached to the minutes of the foreshadowed Canine Health Committee meeting, but that meeting did not eventuate.

A key component of the program is accurate DNA sample collection. The procedure for DNA sample collection is fundamental in ensuring accuracy in the first and succeeding generations: -

- it is essential that the dog presenting for sampling is positively identified, to prevent substitution or accidental mistakes
- collection of the sample must be by independent persons to ensure the dog presenting is as purported
- collectors must be trained – while taking the sample is a very simple process it is easy to make mistakes in dogs sampled and paperwork unless correct disciplines are in place.

Collection may be achieved by various routes: -

- GTG will provide full collection services on their own initiative and on request
- Member Bodies, with the opportunity to generate income from taking part in the collection and processing should they so desire, which needs to be discussed individually and promptly
- breed clubs and other canine organisations, with the opportunity to obtain volume discounts or generate income through holding collection days and having their own approved collectors.
- veterinarians are automatically qualified to collect
- microchip implanters are a logical vehicle
- individual persons may also be approved, eg. on a geographic basis.

GTG has had applicants from all over Australia and seeks approval by Member Bodies, breed clubs or other canine organisations to aid in selection. GTG will ensure all collectors are trained and provide each with a microchip scanner where necessary.

**Conclusion**

The program is based on logic, common sense and the use of science to achieve results. It will work if we give it the support it deserves. Key components of the program include GTG as service provider for DNA profiling and parentage testing, together with its range of lower cost hereditary disease genetic tests.

A. R. Maver August, 2005

**Appendix**

## Analysis of Costs and Benefits to Breeders

### General

- The ANKC program is designed to cover breeding stock only, but any dog eligible for the Main Register may participate at the option of the owner
- for ANKC recognition, dogs must have positive identification by microchip or tattoo (note microchips are likely to be compulsory for all dogs in all areas by December 2007) and the cost of this is not included here

### DNA profiling/parentage testing

- the cost of DNA sample collection, sample storage for future use, profiling, parentage checking (where parents' profiles are on the database) and certificate issue, subject to discounts $ 65
- the benefits are that breeders are sure the breeding stock are as purported

### Genetic disease testing

- the cost of a DNA test , depending on the test and whether DNA sample collection is included (the one sample is adequate for disease tests, profiling and storage for future use), subject to discounts $165*
- benefits are accurate information on disease status and ability to prevent disease occurrence in offspring

### Disease clearance by parentage

- where both parents have clear status for a specific disease, an offspring may be cleared of the disease by profiling and parentage confirmation, per offspring, discounts apply $ 65
- benefit is that, in the main, the higher cost disease testing becomes a one-generation cost, replaced by the low cost profiling/parentage test

* Note: This cost is for direct tests and may vary where patent royalties are paid to other parties. Linkage tests (if offered for special circumstances) will be at higher costs due to the nature of the tests.