



TNS Research Update Report

21 May 2007

The donations in 2006 to TNS research from the Border Collie Clubs of NSW, Vic and Qld and several generous breeders from Australia and US came at a critical time and has allowed us to continue the work which has identified the TNS gene and found what appears to be the mutation responsible for the disease. This work was not possible without the samples from litters with affected pups that were provided by breeders. The enthusiastic work of breeders to spread the word about the problem and the research has led to the attraction of funds from the UK Pastoral Breed Health Foundation which had set aside funds to support genetic research in working dogs. Together these funds have allowed us to make rapid progress toward our main aim, which was to identify the TNS mutation, and to examine its distribution in Border Collies around the world.

The funding has provided the consumables we need to do the lab work and the PBHF funds provide a PhD Scholarship for Jeremy Shearman, which now allows him to work full time on the project. The support has allowed him to examine nearly all of the TNS gene in 2 TNS affected dogs and 2 carriers and several controls in just 6 months. He has tested about 30,000 DNA bases that make up the functional part of the TNS gene and has found what appears to be the mutation that causes the disease. We need to confirm this by showing that the mutation exists in the large number of affecteds and carriers that we have already tested, and not in unrelated unaffected dogs. To do this we need to develop a cost effective, efficient test for the mutation. Once we have shown that this DNA difference is the cause of TNS in all known carriers, we will check that all of the dogs predicted to carry the mutated TNS gene by our previous test examining segregation of chromosomes in TNS related animals is 100% accurate. We will also screen samples that showed no sign of TNS to confirm that no other chromosome types also carry the TNS mutation.

The identification of what is very likely the TNS mutation means that we can now test any dog for TNS. Dogs to be tested no longer have to be related to known TNS carriers. Information on samples submitted for testing and test results are kept confidential by us and owners are encouraged to publish their results on the Border Collie Health web site. This means that not all of the test results are generally available yet.

This good news of identifying the TNS mutation is well timed as it balances the bad news that the application for funding of this research through an ARC Linkage Grant was not successful. We will continue to rely on donations and funds raised from our DNA testing to fund further research in Border Collies and other breeds.

Since February, we have typed 800 samples to reveal 180 carriers and 2 affecteds. Twenty-one of the carriers were from recent litters. We have identified 7 carriers from English ISDS lines to date. This supports the unconfirmed TNS cases from ISDS lines on the Border Collie

Health Website as true TNS. It also indicates the mutation is very old and has been around in the breed for a very long time.

Testing has been difficult on a small proportion of samples. This has led to a small number of revisions of preliminary test results. Some buccal swabs do not provide enough DNA for testing and so blood samples are preferred. Poor quality of sample leads to delays in results and are much more likely to produce errors. It is hoped that the new test being developed will allow testing of even the poor samples that have been submitted.

Any samples will now be accepted for TNS testing at UNSW. Forms are available on the Border Collie Health website, <http://bordercolliehealth.com>, on the TNS page. Once samples arrive in the lab it takes two to three weeks to enter details into the database, run tests, and send out results by email, so plan testing accordingly. The preferred sample locally is blood in EDTA tubes which must be packaged properly to send in the mail. Blood on FTA cards is more convenient for international samples. Mouth swabs can be sent from puppies at just a few days old but a proportion (~10%) of swabs do not work so results cannot be guaranteed and duplicate swabs are recommended.

DNA testing of genetic diseases such as TNS, allows breeders to continue to use carrier animals in matings (if mated to TNS clear animals) and test the progeny for carrier status. This means no desired breeding lines need be lost and breeders can still select the best puppies to keep for breeding without any further risk of producing TNS affected animals. Over a period of several generations the disease can be eliminated from the breed by testing and selected breeding. Then testing will be no longer necessary. TNS is inherited as a recessive disorder like CL and CEA. If both parents are tested clear of TNS then their progeny must be also free of the TNS mutation. In matings where one parent is a TNS carrier, about half of the pups, on average, can be expected to be carriers. In some litters all pups will be carriers and in others none will be, but each pup has a 50:50 chance of being a carrier if one parent is. For each puppy from matings between two carriers, there is a 1 in 4 chance it will be affected, a 1 in 4 chance it will be clear of TNS, and a 1 in 2 chance it will be a carrier. But such matings can result in any combination of affected, carrier and normal pups. For example, one litter had 4 affected, 3 carriers and 1 clear puppy.

TNS has most likely been in the Border Collie breed since it originated as it occurs in several lines that are only distantly related. It occurs in show dogs originating from Australia/New Zealand, in pure English working dogs and in Australian working dogs that are unrelated to the show dogs. The disease can present as very different symptoms from one affected litter to another which has made it difficult to recognise as a genetic problem. It is probably the major cause of “fading” or “failing” puppies. Now a DNA test exists there should never be another puppy affected by TNS and eventually TNS can be eliminated from the breed. The purpose of this research, undertaken at University of New South Wales in Sydney, has been to assist breeders improve the health and welfare of the dogs. A side benefit is that the research could also assist in the knowledge and treatment of the disease in human patients.

Testing is currently only available at UNSW where the TNS and CL tests have been developed. The research into developing a more widely available TNS test and determining the prevalence of TNS in the breeding population continues to be done by PhD student, Jeremy Shearman. Without the support of the breeders and owners, the amazing progress Jeremy has made in a short time would not have been possible and his work could not continue.

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