

Identifying the Mutation Causing Lens Luxation in the Tibetan Terrier
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SUMMARY TO BREEDERS:

In this study we have looked for the mutation causing Lens Luxation in Tibetan Terriers. First, we asked whether Tibetan Terriers suffering Lens Luxation have the same genetic region affected as other breeds. To do this we looked at highly variable DNA sequences (known as microsatellite alleles) in luxated animals. We showed that in a region of chromosome three, the alleles present in luxated animals were different from those in the whole population. This region was previously implicated in luxated animals in three other breeds (Jack Russell terrier, miniature bull terrier, Lancashire heeler (aka Ormskirk terrier). This suggested that the same gene or genes might be affected. We narrowed the region somewhat using a technique (“SNP mapping”) that looks for single base changes in the genome, but the detailed study has only served to show that the situation is more complex than we had anticipated. It seems possible that Lens Luxation can sometimes occur even in expected carrier animals, and possible that more than one variant of the gene may cause the mutant phenotype. We have completed sequence of all the protein coding regions of genes within the most highly implicated area and have not found any changes that could cause disease. A region implicated as controlling one candidate gene cannot be easily manipulated using enzyme based techniques, nor sequenced by standard chemistries. (This is fairly uncommon but by no means rare in these types of regions. It implies an unusual base sequence leading to a departure from standard double helical structure.) It may be that further work with this region will tell us more.

In the meantime we are continuing to explore the possibility of developing a ‘linkage-based’ DNA test that would use the DNA within the PLL critical region to determine whether dogs are affected, carrier or clear of PLL. Because linkage-based tests do not assay for the presence or absence of the causal mutation, but rather rely on nearby ‘linked’ DNA, they are not 100% accurate, but if carefully designed they can achieve levels of accuracy in excess of 95% and would represent a useful tool with which breeders can start to reduce the incidence of this condition until the mutation itself is identified. However at the moment this tool seems closer for the Lancashire Heeler than for the Tibetan Terrier. We continue to require more affected and particularly more control DNA samples (blood or cheek swab) from elderly Tibetan terriers with normal eyes, in order to further progress this study. A submission form is available from drs20@cam.ac.uk.