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Update on CA in Working Kelpies

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In 2012, the cerebellar abiotrophy (CA) project in working kelpies was reinstated in the Faculty of Veterinary Science at the University of Sydney with a new team: Peter Williamson, Claire Wade, Rosanne Taylor and Annie Pan. This was made possible by a three-year Australian Post-Graduate Award from The University of Sydney to Annie, the generous donation of $10,000 towards the project from the Working Kelpie Council and a research grant ($7,500) from the Australian Companion Animal Health Foundation.

Substantial progress has been made over the past 6 months towards analysing DNA from CA working kelpies and to compare this with healthy dogs (referred to as the mapping project). We have now genotyped over 170,000 sites (SNP) in the genomes of 99 kelpies, including 30 CA affected and 47 unaffected working kelpies, with the remainder coming from a comparative kelpie cohort included in the Farm Dog Behaviour Project. Analysis of the data collected from these genotypes has revealed five sites on separate chromosomes (chromosomes 3, 22, 34, 35 and X) which have not been previously identified in relation to CA. A close examination of the region around these sites revealed that 77% of the affected working kelpies had the “risk” genotype at one or more sites, with 23% of CA cases still unexplained by any these. The risk genotype on chromosome 35 was only found in a family of CA cases (n = 4) that were resident in Germany, but bred from Australian-imported working kelpies. These results suggest that CA in working kelpies is not a single gene condition, and that different family lines may be carrying different mutations. We have recently submitted a paper based around these findings from the CA gene mapping project, to an animal genetics journal.

We have identified the genes most likely to be involved in the disease for each of these regions and are continuing to analyse the relevant DNA sequences. We are now using entire genome sequences of six kelpies from the Farm Dog Behaviour Project, and have complete one CA case with two others in progress. This data is used to search for functional DNA changes in the identified regions (on chromosomes 3, 22, 34, 35 and X) that may cause CA. This approach has so far identified a number of gene variants that will be evaluated as CA candidates. This is a painstaking task that will continue over coming months. The end-point of this process is a genotyping test or series of tests that will allow us to assess a dog’s risk of having CA. Additionally, we may expect that dogs with established CA ancestry may be tested for the presence of the affected gene unique to that line.

The complexity of CA is also being addressed using detailed clinical and pathological information. This is critical to unravelling the variation in disease presentation and genetics. We added six new cases to this study in 2013, bringing the total to 15 cases with detailed clinical and/or pathological information. The material collected allows us to follow changes in cells and molecules in the brains of CA affected dogs that may be contributing to disease. We are in the process of analysing these data for collation into a report.

Finding the genetic cause of CA in working kelpies is a complex challenge but we are convinced that this systematic approach to defining the disease alongside detailed genetic characterisation is the best approach towards finding a solution.

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