



Rosanne Taylor
Dean, Faculty of Veterinary Science

17th September 2013

Progress Report: CA in Kelpies

Annie Pan, Prof. Claire Wade, Prof. Rosanne Taylor, and A/Prof. Peter Williamson.
Faculty of Veterinary Science. The University of Sydney.

The late Associate Professor Alan Wilton and his research team (Dr. Jeremy Shearman, and Ms. Annie Pan) at the University of New South Wales have put in an extensive effort in the past (2007-2011) to determine the genetic basis of cerebellar abiotrophy (CA) in Australian Kelpie dogs. However, identification of a genetic cause of the disease proved to be elusive, and there is still no test to identify dogs that are affected.

In 2012, this project was reinstated in the Faculty of Veterinary Science at the University of Sydney. The project has continued with a new team: Peter Williamson, Claire Wade, Rosanne Taylor and Annie Pan. This was made possible by the award of a 3-year PhD scholarship to Annie, and the generous donation of \$10,000 towards the project from the Working Kelpie Council.

The study has opened in two areas, searching for new cases to add to the few clearly defined cases that already were identified. There is a continued need to make sure that we can define the pathology and neurological aspects of CA, otherwise genetic analysis to identify a cause will be impossible. The second area of the study is to analyse DNA from CA dogs and to compare this with healthy dogs (referred to as the mapping project). Since continuing with the mapping project, we have genotyped 25 CA affected and 16 related unaffected Kelpies using the high density genotyping arrays made by Illumina. Analysing the data collected from these genotyping arrays has revealed a strong disease associated signal on chromosome 22 that was not previously identified as an area where a mutated gene may be found. When we looked closely at this region we found that only 32% of the affected Kelpies genotyped had this genotype. Multiple signals of less significance were found to be dispersed on different chromosomes among the remaining 68% of affected Kelpies. This result suggests that, either CA in the Kelpie is caused by a number of mutations and different lines carry different mutations, or a combination of mutations add together to cause disease in each dog.



THE UNIVERSITY OF
SYDNEY

We are currently investigating a number of candidate genes from those regions identified for possible causative variants using DNA sequencing. In parallel, we are undertaking detailed histopathological studies to define the neurological phenotype for any Kelpie enrolled in the study, and for newly identified cases. This work will also allow us to better understand the way the disorder develops. Some of this work was recently presented at the Genetics Society of AustralAsia Conference held at the University of New South Wales, (July 14-17).

We have most recently benefited from a huge amount of data from entire genome sequences of a number of Kelpies from a parallel study by Prof Wade, and which included one CA case. This will identify all possible gene variants associated with CA. Analysis of this data is a big task, and will continue over coming months.

Finding the genetic cause of CA is a complex challenge but we are convinced that this systematic approach to define the phenotype and continue with detailed genetic characterization is the best approach towards developing a DNA test. Finally we received some further good news in July, with the award of a small research grant from the Australian Companion Animal Health Foundation (\$7,500) to help cover the costs of genetic analysis.

Please visit us at: <http://sydney.edu.au/vetscience/about/students/annie-pan.shtml>, and/or at our Facebook page: <https://www.facebook.com/CA.Kelpies>.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Rosanne Taylor'.

Rosanne Taylor