

## **SYRINGOMYELIA NEWS**

**2006**

### **A research update**

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### **Full CKCS Genome Scan for both Syringomyelia and Mitral Valve Disease**

It is two years since we started to produce our research newsletters and we are proud to be able to report that a full genome scan looking for the causal gene/s of syringomyelia and mitral valve disease is underway! This follows the success of the international blood collection “DNA for Healthy Cavaliers” for which so many individuals contributed.

Dr Zoha Kibar –at Centre for the Study of Brain Diseases, CHUM – Montreal reports:

Both Syringomyelia and Mitral valve disease are particularly common in the Cavaliers. Such high incidence in a particular breed as compared to other breeds suggests the involvement of genetic factors. The mode of inheritance including the number, identity and relative contribution of the causative genes is not determined yet. The etiology of both conditions could be further complicated by variable penetrance of the various genotypes and the involvement of environmental factors.

The first step which is genetic mapping is currently underway. Due to the complex inbreeding in the CKCS, a preliminary genetic analysis was necessary to evaluate the informativeness of the genetic markers and hence the feasibility of a whole genome scan in such breed. Consequently, 10 dogs were selected for genotyping with 122 markers distributed among the 38 autosomes and X chromosome. The markers were found to be sufficiently polymorphic and informative. Next, 200 dogs were selected for a whole genome scan, primarily for Chiari malformation. However with additional phenotypic information on mitral valve disease, it is possible to use the same data to map the gene(s) defective in this disease. The whole genome scan was conducted at the Mammalian genotyping Center at the Marshfield Clinic in Wisconsin, USA. The genotyping data will now be analyzed using both linkage-based and association studies. In the latter, we will be taking advantage of the founder effect demonstrated for both these disorders in the CKCS breed.

This strategy involves: 1) genetic mapping of the underlying gene(s), 2) identification of these defective gene(s) using the positional candidate gene approach and characterization of the mutation(s) and 3) initial functional characterization of the protein(s) encoded by the gene(s). This will help better understand the underlying pathogenic mechanisms for better diagnosis, prognosis and clinical management of these devastating conditions. These studies will also help unravel some of the complexity involved in this malformation in humans and in the embryonic

development of the affected structures.

## **Research Team**

We are sorry to announce that Melanie Benard has moved on and would like to take this opportunity to thank her for her hard work and tenacity. Her experience working in the human genetics was paramount when dealing with the vast numbers of dogs and samples. The UK Archive ( Manchester) who extracted the DNA at their own expense sent 3 small samples for each dog i.e. well over 1,500 samples and it was Melanie who ensured that none went astray.

Her successor is Isabelle Thibault, who we welcome. Her address is

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We are proud to be working with Dr Yan Yang who has recently joined Dr Rouleau's Genomic Unit at the Centre for the Study of Brain Diseases. She first graduated in medicine, later did research at the Molecular Oncology group in McGill and now has included Bioinformatics database in her multidisciplinary career.

## **Support from The Cavalier Club, UK**

The Club will be funding a research project by Clare Rusbridge and Dr Nick Jeffery (Cambridge University) that is designed to establish whether the position of the dog's head in the MRI receiving coil could affect the apparent severity of the malformations associated with syringomyelia in the cavalier King Charles spaniel. This is with the aim of making future recommendations for MRI screening. Further information about this can be found at [www.sm.cavaliertalk.com](http://www.sm.cavaliertalk.com)

A Syringomyelia seminar was given by Clare at the Wood Green Animal Shelter, Godmanchester on Dec 11th 2005. Thanks go to Mrs Margaret Carter and Mrs Jeannie Boyd for organising this. It addressed issues that were relevant to breeders, pet owners and the veterinary profession. A DVD of the talk (£10/\$20 including P&P) is available from [penny.knowler@ntlworld.com](mailto:penny.knowler@ntlworld.com). or [info@cavaliertalk.com](mailto:info@cavaliertalk.com)

A sensitive book 'For the Love of Ollie' by Sandy Smith has been written to raise awareness to syringomyelia and how it impacts on people's lives. Please visit <http://www.fortheloveofollie.com/> for details. The site provides information and support.

All proceeds from both these initiatives go to Syringomyelia DNA Research.