Genetic studies of Chiari-like Malformation with Syringomyelia (CM/SM) in the Cavalier King Charles Spaniels (CKCS)

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This study was initiated in 2000 when research suggested a possible hereditary basis for CM/SM. We have constructed a genealogy and database which currently holds 10,600 related CKCS dogs spanning 24 generations from over 700 MRI confirmed dogs with relevant phenotypic information.

A grant from Cavalier Health Foundation (#104) was obtained in 2003 with the purpose of archiving CKCS DNA. This was in collaboration with **Dr Guy Rouleau at** Director of **CHU Sainte Justine Research Centre in Montreal** (formally at McGill University**)** and **Dr Berge Minassian at the Children's Hospital Toronto.** With sponsorship from the UK DNA Archive, Boehringer Ingelheim UK, Utrecht University, the Cavalier Club UK and TDDS Laboratories we have now collected over 1,500 DNA samples worldwide. The collection is known as 'DNA for Healthy Cavaliers'. The campaign has been supported by a huge number of dedicated dog owners, breeders and veterinarians in Europe (especially the Netherlands), USA, Canada, Australia and South Africa. We are indebted to all those providing information, blood samples and to a variety of imaginative fundraising initiatives e.g. Sandy Smith's book 'For the Love of Ollie'.

The current genetic investigation is led by **Dr Zoha Kibar** at **Sainte Justine Research Centre.** An initial CKCS whole genome scan was completed in 2005 with 173 CKCS dogs – selection was based on SM-affected status and familial relationship in the CKCS database. Genetic analysis was undertaken by **Dr Marie-Pierre Dube at University of Montreal** and identified six genomic regions that could harbour the CM/SM gene(s).

A recent grant from the **American Kennel Club Health Foundation (#954)** with matching funds provided **by ACKCSC and Cavalier Club of the USA** has allowed our genetic studies to continue. Dr Kibar is undertaking the fine mapping of the six genomic regions with a larger sample size. Additional DNA samples have been provided by **North Carolina State University** and **Guelph University** as a side study from their own investigations into CM/SM. A new whole genome scan using the innovative canine SNP (single nucleotide polymorphisms) genotyping technology is planned in the near future. The candidate genetic interval(s) identified in both genome scans will be narrowed down using genetic studies in the CKCS and other toy breeds affected with CM/SM including information from our collaborative research at **Georgia University** (AK CHF grant #1004) Once the candidate genomic region(s) have been well defined, the positional candidate gene approach will be used to identify the defective gene(s) in CM/SM.

Finding the gene/s responsible for CM/SM will help better understand the underlying molecular and cellular pathogenic mechanisms for better diagnosis, prognosis and clinical management of the conditions. As an imminent outcome it will be possible to develop a genetic test to identify carriers and devise breeding strategies to reduce or eliminate this devastating condition in the CKCS and other affected breeds. We are collaborating with **Dr Sarah Blott** at **the Animal Health Trust** in the UK who is developing an optimization breeding programme for dogs aimed to help breeders breed away from the condition.