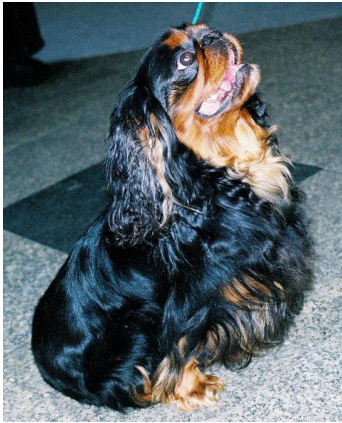


Research into Chiari-like Malformation

Story so far.....

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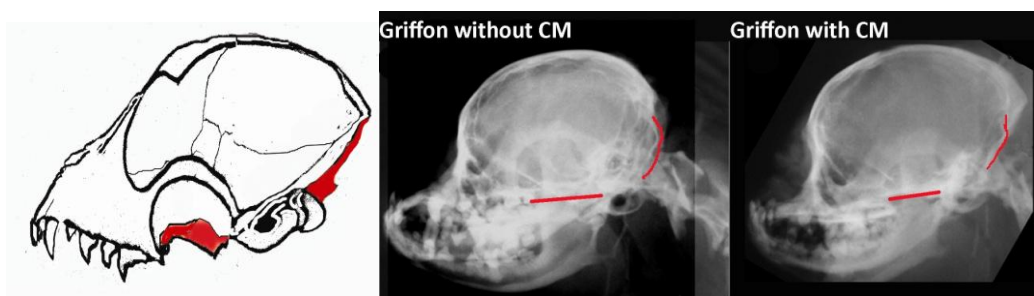
Background

Chiari-like Malformation (CM) is characterized by overcrowding of the back of the skull (caudal fossa) due to a combination of a proportionally small volume skull and large brain. Like humans sufferers with chiari malformation, dogs can suffer pain especially if they develop syringomyelia (SM). The genetic research for SM is being investigated in the Cavalier King Charles Spaniel ([here for latest update](#))

Many small breeds (and toy cross breeds) are affected by CM

CKCS	Cavalier King Charles Spaniel
miniaturisation	Yorkshire terrier, Pomeranian, Maltese terrier, Chihuahua
brachycephalic	King Charles (KC), Griffon Bruxellois, Affenpinscher, French bulldog, English bulldog, Pug
other breeds	Havanese, Norfolk terrier, Boston terrier, Bichon Frise, Staffordshire bull terrier
crossbreeds	CKCS x Pomeranian, CKCS x KC, CKCS x Shih Tzu, Yorkie crossbreed

Thanks to dedicated breeders and owners who recognise the importance and significance of current health concerns in the breed, CM is currently being investigated in the Griffon Bruxellois. The bones involved in CM (coloured red in the diagram below) are embedded in muscles and it is impossible to measure the compression of the hindbrain without specialized equipment such as magnetic resonance imaging (MRI)



Research using radiographs above ([click here for more details](#)) suggests that dogs with CM appear to have reduced bones at the base and back of the skull and where the spinal cord exits the brain (called the caudal fossa). It is thought there is compensatory growth of the other skull bones to accommodate the fore brain but the hind brain and cerebellum) is left with insufficient space. The bones of the base of the skull and caudal fossa have a different embryological origin to the bones that form the roof of the skull. The theory suggests that during development of the embryo, these cartilaginous bones are perhaps deficient in dogs with CM or that the plates of bones involved fuse earlier so preventing further growth (craniosynostosis). Early results from studies have also suggested that the brain in SM affected CKCS

is also disproportionately large. It is hoped that the study into foetal tissue at the Royal Veterinary College will help elucidate this.



Skull volume in Cavaliers – When Cavalier dogs of all ages were investigated for CM there is no difference between the volume of the skull (caudal fossa) of those that had Syringomyelia (SM) and those that did not have SM. However, when age was taken into consideration, the volume of the skull was significantly smaller in young cavaliers with early onset SM (under 2y) compared to cavaliers clear of SM over 5 years of age. Also the size (volume) of brain within the skull was significantly greater in SM cases and even greater in young dogs with early SM cases.

Genetic research into Canine chiari

Principal Investigators are Dr Clare Rusbridge and Penny Knowler at the Stone Lion Veterinary Hospital and the geneticists Drs Zoha Kibar and Guy Rouleau at the CHU Sainte-Justine Research Center, University de Montréal. Canine Chiari-like malformation (CM) is the only known naturally-occurring animal model for the condition in humans **Chiari type 1 malformation** (CM-1) and represents a powerful tool for deciphering its complex genetic etiology. The team aims to identify the CM gene(s) in the dog which will provide an entry point for identifying equivalent genes involved in CM-I in humans. Understanding the genetics will allow better understanding of the cause and what treatment / management would be best for both humans and dogs

In 2007 we conducted a scan of the whole dog genome on normal and CM affected Griffon Bruxellois and other related breeds using the CanineSNP20 BeadChip array. The latter represents a multi-sample array which contains over 22,000 highly informative single nucleotide polymorphism probes (SNPs) developed across the whole dog genome. The initial samples were from **Australia** with additional samples from the **UK, Netherlands, Finland** and **USA**. This project would not have got off the ground if it wasn't for cavalier pet owner Sandy Smith's '**For the Love of Ollie Fund**' from **Canada** and contributions made to the **SM DNA Research Fund** and Lee and Frank Pieterse in Australia.

Case-control association studies showed significant association of the CM disease with two SNPs on 2 chromosomes. Put more simply so far the genetic studies have suggested that the CM gene(s) might be localised to small regions on these chromosomes but we have yet to prove it definitely. Thanks to generous funding by the **Ann Conroy Trust** we are able to take the next step which is to investigate these two chromosomal regions for true association to CM by additional genetic studies in a larger group of 175 Griffon Bruxellois and other breeds with CM.

We now have a worldwide DNA database of 235 MRI confirmed status for CM affected dogs and unaffected Griffons included 72 samples from **Dr Simon Platt at University of Georgia USA**. This welcome boost to CM/SM research in the Griffon made possible from a grant from the American Kennel Club, matched by the Griffon Clubs of the USA, Australia, UK and NZ. It will not doubt make a significant contribution to further understanding of this complex condition.

Support is international Thanks to many UK members of the [Griffon Bruxellois Club 1897](#) and [Griffon Bruxellois Breeders Association](#), co-ordinated by Maria Oliver and Tessa Gaines. In the Netherlands we had the help and support of Hans Bleeker and [Henny van der Berg](#). Many breeders travel long distances to MRI their dogs and make huge efforts to ensure that samples arrive safely including those from [Russia](#) and [Norway](#). For example Riikka Velling managed to ship blood samples that were time urgent when the country was buried in unusually deep snow conditions! Thanks to her and many other members of [The Griffon Club in Finland](#) co-ordinated by Hannele Åfelt.



Working together and making a difference

It is enormously satisfying to work with breeders and pet owners who obviously have a deep love of their breed and concern for their welfare. We should like to take this opportunity to thank everyone – vets, breeders and owners who have helped the research effort or raised awareness.

Fundraising is essential for research of any kind but particularly for CM/SM where the cost of MRIs to confirm the diagnosis causes an increased financial burden. [‘SM DNA Research’](#) has funded over 20 important MRIs for some key dogs for the genome research from Finland, Netherlands, UK, USA, Australian and New Zealand. Contributions made to this fund are almost entirely from the [Cavalier lovers](#) since CM has a high incidence in their breed.

Thanks to Rachael Harvey there is now a dedicated website for breeds with CM/SM. Visit [Friends of Lola](#) for more information about the imaginative efforts from sponsored events, sales of artwork, garden fetes, etc., [Friends of Lola Fund](#) is being used to MRI dogs who are considered to be **WITHOUT CM**. Identifying such dogs will also boost the numbers of CM unaffected dogs for breeding purposes.

FREE MRI AVAILABLE

YOU can help. You may know a dog that can help the research or simply make a financial contribution to the research funds – every little helps.

Please get in touch with [Dr Rusbridge](#) or Penny Knowler for details of free MRI or if you have

- **Griffon that has been MRI'd and has no CM**
- **Other toy breed with an MRI of the brain and upper spine with or without CMSM.**



The future. CM is a complex trait involving the interaction of genes and until the genetic cause is found the only way to confirm CM status is an expensive MRI. [The BVA/KC MRI screening scheme](#) has been set up in response to breeders' request for consistent and reliable MRI interpretation. The protocol aims to ensure CM and SM can both be reported and suggests breeding guidelines until a computerised breed selection programme becomes available.