Penn Veterinary Medicine

Margret L. Casal, Dr med vet, PhD, Dipl. ECAR
Professor of Medical Genetics, Reproduction and Pediatrics
Section of Medical Genetics, CS&AM

Renal Dysplasia in the Cairn Terrier
Progress Report

Progress

The aim of this research project has been to investigate the inheritance of renal dysplasia in the Cairn terrier breed and the degree to which genetics influences the severity of disease - whether it is mild, moderate, or severe. We have examined several pedigrees which, together, detail the ancestry of approximately 1500 Cairn Terriers; performed ultrasounds of the kidneys of over 500 dogs; and collected DNA from about 300 dogs. The affected samples made up about 10% of all DNA samples, suggesting that there are about 42% carriers in the population. Two thirds of all affected dogs could be directly linked to a single common ancestor. However, this is not an uncommon finding in a purebred dog population. It does point out though, that until we have a DNA test available, one should aim for having an ultrasound of the kidneys performed by a board-certified veterinary imaging specialist before making breeding decisions. We have performed the first and second run of our genome wide association study and are currently re-analyzing the data, as several of the ultrasound images had to be re-analyzed due to misclassification. The review of these images has been completed and the dogs properly classified. We had sent DNA samples from two affected dogs for a whole genome sequence to be able to accurately pinpoint the difference between dogs affected with renal dysplasia and "clear" dogs. However, the sequencing failed, and we need to resubmit a sample. Covid-19 has slowed down this process tremendously but now that we are hopeful for a return to normalcy soon, we can speed up our efforts, provided we obtain extra funding for the sequencing.

Significance of Findings

1. Dogs' kidneys are incompletely developed at birth and continue maturing over the 3-4 months of life. If you were to look at biopsies of the kidney, you would see some fetal structures (glomeruli) still present during the first weeks of life. On ultrasound, the ratio of cortex (the outer part of the kidney) to medulla (inner part) changing dramatically during the first months of life. Therefore, it is important to note that ultrasounds to assess the health of the kidney for screening purposes should not be performed until 12 weeks of life to provide an accurate diagnosis.
2. Renal dysplasia is a complex disease, meaning that it does not follow a simple mode of inheritance. With all the information that we have so far, it appears that it is one major gene that is responsible for the disorder but there are likely 1-2 modifier genes that change the severity of renal dysplasia in an affected dog.

Final Comment

We are extremely grateful to the Cairn Terrier Club of America for all of the assistance thus far. We are thrilled with the number of participants and could not have gotten as far as we have without their help in trying to unravel this complicated disease!
We are equally grateful to all veterinarians that have sent us images plus the reports of Cairn Terrier seen at other institutions and practices.

Results and Impact

We expect this project to result in the discovery of a major variant that is associated with renal dysplasia in the Cairn Terrier, thus enabling breeders to plan their breeding programs without the fear of producing affected puppies. The discovery of a disease-causing variant will also aide in understanding the mechanism of disease, which will not only be helpful in the development of a potential therapy for affected dogs but also in people.

University of Pennsylvania School of Veterinary Medicine • 3900 Delancey Street • Philadelphia, PA 19104-6010
Tel 215.898.0029 • Fax 215.573.2162 • casalml@vet.upenn.edu