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Genetics of Human and Canine Dilated Cardiomyopathy

We would like to provide a summary of our recently published paper 'Genetics of Human and Canine Dilated Cardiomyopathy' http://dx.doi.org/10.1155/2015/204823. This paper is a review of the current state of genetic research into canine DCM, with comparisons with the research into human DCM.

Dilated cardiomyopathy (DCM) is the second most prevalent form of canine heart disease and is estimated to be the third most common type of inherited human heart disease. Clinically human and canine DCM are similar, often leading to heart failure and death. Treatment for both canine and human DCM is similar with drugs used to delay disease progression and minimise the effect of heart failure to maintain a good quality of life, but there is no cure. There is, however, an additional option available to treat human, but not canine DCM – a heart transplant.

There are many possible causes of DCM, but in humans there is often a genetic cause. The genetic cause of human DCM can be restricted to a single family afflicted with the disease. Similar to this there are some dog breeds which are particularly affected by DCM. Dog breeds can be considered large families with individuals within a breed more related to each other than between breeds. When families or breeds have a high prevalence of a disease it indicates that at least part of the cause is genetic. Canine DCM particularly affects some breeds including Irish Wolfhounds, Deerhounds, Great Danes, Newfoundlands, St. Bernards, Doberman Pinschers, Boxers, and English Cocker Spaniels, indicating that the cause of the disease within these breeds is likely to be genetic and, as with human familial DCM, it may be different between breeds.

There is some evidence for different types of canine DCM, as with different types of human DCM. This evidence is drawn from the age of onset of disease, cellular changes visible with a microscope observed post mortem, inheritance pattern, disease progression and prognosis following diagnosis. These clinical features are discussed within the paper for the breeds where possible genetic causes of canine DCM have been identified (Boxers, Doberman Pinschers, German Short-Haired Pointers and Irish Wolfhounds). We suggest that if the different types of canine DCM can be clinically matched to the different types of human DCM they can act as models for each other with regards to identifying the genetic basis and the best treatment of the disease. This is not yet possible as the different types of canine DCM in particular need to be better described.

There have been many studies into the genetic basis of canine DCM, but very few, so far, have found a genetic association. In our paper we discuss the possible reasons for this including: sample size, inappropriate controls, and type of study, and make the recommendations for future studies. A brief overview of these recommendations are:

> Many studies into canine DCM have been small with only 5-40 individuals. Unless the size of the genetic effect is very large this is not big enough to detect an association. Genetic effects relate to how big a part of disease development is due to the gene being examined. The studies which have identified genetic associations have used larger sample sizes; however, the size of the effect they have identified is still moderately large (0.2-0.4). Most genetic effects are small (0.1 or less) and we estimated the minimum number of samples required to

detect an effect of 0.1 is 785. This is the minimum number of samples that studies into the genetic basis of canine DCM should aim for wherever possible.

All studies into the genetic basis of diseases require appropriate controls to compare the genetics of affected individuals with the genetics of unaffected individuals. Controls should be from the same population and ensure that they have not got or will not develop the disease of interest in the future– an individual's genetics stays the same throughout life, but diseases don't. In the case of canine DCM, controls should be from the same breed and be old enough to be confident that they are unlikely to develop DCM, this age is based on common age of diagnosis within the breed.

Many studies into the genetics of canine DCM have examined the canine version of genes associated with human DCM. Even within human DCM there is not a single gene that causes the disease, it is therefore not surprising that very few studies have found a genetic association with canine DCM. This is particularly true when the other problems of sample size and appropriate controls are included. Successful canine DCM genetic associations have been made when the whole genome has been examined rather than just a small part, combined with larger sample sizes and appropriate controls.

In conclusion, the paper discusses the clinical features and treatment of human and canine DCM, the possibility of different types of canine DCM, genetic research into human and canine DCM and reasons why canine DCM genetic research lags far behind that in humans. In addition we make suggestions to improve future studies into the genetic basis of canine DCM.

Please feel free to visit the published paper by our group at:
http://dx.doi.org/10.1155/2015/204823

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