



Animal *Health* Trust
Oncology Research Group

Research study to identify Genetic Risk Factors for Mast Cell Tumours in Golden Retrievers

With the invaluable support of the Golden Retriever Breed Council, in the autumn of 2009 the Oncology Research Group at the AHT was successful with an application to the Kennel Club Charitable Trust for funding for a study to identify inherited genetic alterations responsible for European Golden Retrievers having an increased susceptibility to developing mast cell tumours. It is hoped that the research will enable the development of a DNA test that can be used to identify individual Golden Retrievers that are more likely to develop mast cell tumours.

Since the study began in January 2010 (and in collaboration with scientists in Sweden, the Netherlands and the United States), we have analysed ('genotyped') DNA samples from 91 Golden Retrievers with mast cell tumours, and 90 Golden Retrievers aged at least 7 years old that have never had a mast cell tumour. The aim is to find genetic markers (called 'SNPs'), amongst the 170,000 SNPs that we look at in each DNA sample, that are present much more frequently (than would be expected by chance) in the DNA of Golden Retrievers with mast cell tumours. We found several such SNPs located in an extremely large region on one chromosome, and this result suggests that the region (about 23% of the overall size of the chromosome) contains one, or more, genetic alterations that cause an increased risk of developing mast cell tumours. Unfortunately, the region is so large that it contains 323 genes (the parts of DNA that have a function), and so there is still considerable work to be done to identify which of the genes contain a genetic alteration.

Pinpointing the genetic alterations may be assisted by the results from a parallel study, conducted by our collaborators in the United States (US), on US Golden Retrievers. The US study suggested that there may be genetic alterations associated with an increased risk of developing mast cell tumours on a different chromosome in US Golden Retrievers. Although the regions in the European and US Golden Retrievers are different, they contain genes that are related. We don't believe that this is a coincidence, but rather that this suggests that the genetic alterations will be found in these genes, and so these genes are at the centre of current efforts to identify the precise genetic alteration(s) that confer an increased risk of developing mast cell tumours.

In order to pinpoint the genetic alteration(s) we have 'decoded' (a process called 'DNA sequencing') the sequence of 'DNA letters', which comprise both the genes of interest and the sections of DNA surrounding the genes of interest, in the DNA from several Golden Retrievers with mast cell tumours and several unaffected Golden Retrievers. We are still analysing the data attempting to identify consistent differences between the 'letters' in the DNA from the Golden Retrievers with mast cell tumours and the 'letters' in the DNA from the unaffected Golden Retrievers. Such differences may represent inherited genetic alterations that cause an increased susceptibility to developing mast cell tumours. Unfortunately, this approach is not straightforward, as it is difficult to prove which genetic alterations may contribute to an increased risk of developing cancer.

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