



Animal Health Trust
Oncology Research Group

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

With the support of the Golden Retriever Breed Council, in January 2010 we began a 'genome-wide association' study seeking to identify inherited genetic alterations responsible for Golden Retrievers having an increased susceptibility to developing mast cell tumours. The primary aim of the study was to begin to understand how inherited genetic alterations contribute to the development of mast cell tumours by Golden Retrievers. This knowledge would ultimately assist the development of new treatments that specifically target the genetic alterations involved in mast cell tumour development. A longer term objective for the study was to potentially enable the development of a DNA test (or DNA tests) that could be used to quantify the risk that an individual Golden Retriever has of developing a mast cell tumour.

Funding from the Kennel Club Charitable Trust enabled us (in collaboration with scientists in Sweden, the Netherlands and the United States) to analyse 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 was to find genetic markers (called 'SNPs'), amongst 170,000 SNPs screened 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 chromosome 20, and this result suggested that the region (over 20% of the overall size of the chromosome) contains one, or more, genetic alterations that cause an increased risk of developing mast cell tumours.

In order to try to pinpoint the genetic alteration(s) the sequence of 'DNA letters' in the candidate region of chromosome 20 was 'decoded' (a process called 'DNA sequencing') in the DNA from 3 Golden Retrievers with mast cell tumours and 4 unaffected Golden Retrievers. As a result of this analysis a genetic alteration in a particular gene (called 'GNAI2') was identified. A parallel study conducted (by our collaborators in the United States) on US Golden Retrievers also suggested that several other genes (called 'hyaluronidase genes'), that are located in the same region of chromosome 20 as GNAI2, may also contain alterations that confer an increased risk of developing mast cell tumours. The US study found that in US Golden Retrievers there may be genetic alterations associated with an increased risk of developing mast cell tumours in a particular region on chromosome 14, which also contains a hyaluronidase gene. We don't believe that this is a coincidence, but rather this suggests that genetic alterations associated with mast cell tumour development will be found in hyaluronidase genes in both European and US Golden Retrievers. This research was published in a scientific journal in 2015 [Arendt *et al.*, 2015. Genome-Wide Association Study of Golden Retrievers Identifies Germ-Line Risk Factors Predisposing to Mast Cell Tumours. PLoS Genetics 11(11): e1005647].

Research is currently ongoing in our Swedish collaborator's laboratory to establish how alteration of the GNAI2 gene may be involved in mast cell tumour development, and investigate whether alterations in hyaluronidase genes may also be involved in promoting mast cell tumour development. Further research at the Animal Health Trust will be dependent upon obtaining new external research funding.

Mike Starkey
Oncology Research Group
October 2016