REPORT OF OCULAR MELANOSIS RESEARCH. September 2019

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The aim of the research is to identify the gene mutation that is causing ocular melanosis in Cairn terriers. Previously we mapped the location of the DNA mutation that causes the condition to a particular region of the genome. This means that we have strong evidence of a location of the mutation on a particular chromosome. This also means that we have narrowed down the location from somewhere in the 3 billion base pairs of DNA that make up the dog genome to a region of about 7 million base pairs. We looked at the known genes in the region and sequenced several of them without finding an alteration that causes the condition. We also looked at gene expression in affected eyes and did not find any differences in the genes that map to this region. We have sequenced the entire genome of several affected Cairn Terriers and control unaffected Cairn terriers. This investigation relies on the published sequence of the dog genome as a "map" to help us locate the mutation by comparing the sequence in the affected and unaffected dogs. This did not reveal any DNA changes that we think cause ocular melanosis. We now have evidence that the canine genome "map" is incorrect in this region and is missing some information. We believe one of the missing regions is the site of the ocular melanosis DNA defect. Conventional genome sequencing is unable to provide sequence information for the missing region in which we believe the mutation causing ocular melanosis is "hidden".

We have now used a newer form of genome sequencing that sequences very long strands of DNA. This form of genome sequencing is useful for identifying errors in the published genome such as regions of DNA that are duplicated. It also is useful to find DNA changes that cause disease such as duplications or inversions of DNA that are difficult to identify by conventional DNA sequencing. Analyzing the sequence information generated by these new methods of DNA sequencing requires a lot of computer analysis and assembling a new genome sequence for individual animals; this is challenging and time consuming. We are in the process of doing this and hope that this will help us identify the DNA change that causes ocular melanosis. So far we have identified several changes that are being studied to see if they are responsible for ocular melanosis.