Investigations into the Genetic Origins of Orthopedic Phenotypes in the Nova Scotia Duck Tolling Retriever

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Introduction

Elbow dysplasia (ED) is a group of conditions resulting in elbow dysfunction. The top three presentations of ED are: fragmented coronoid process (FCP), osteochondrosis dissecans (OCD), and ununited anconeal process (Hayward et al. 2016). The current theories for the pathophysiology of ED in dogs are multifactorial, including genetics, trauma, cartilage/bone defects, nutrition, and others. Despite unknown origins, ED always result in progressive arthritis leading to pain and loss of function. Treatment for ED is limited; surgical options for the management of ED have limited effectiveness and pain management is only partially effective. Therefore, minimizing the impact of ED within the dog population is best accomplished by breeding practices aimed at purging the mutated genes responsible for the defects (Oberbauer et al. 2017). In 2019, Dr. Bannasch and Dr. Marcellin-Little identified 2 adult Nova Scotia Duck Tolling Retrievers (Tollers) with asymptomatic FCP in a CT study looking at phenotypic effects of chondrodystrophy. In this study, we use a genome wide association study (GWAS) to investigate FCP in the NSDTR. In addition, we identify the effects of chondrodystrophy on height in a cohort of NSDTR.

Materials and Methods

The three most common forms of ED are demonstrated in the CT images in Figures 1-3. All forms of ED can occur individually, or in conjunction with one or more of the other manifestations. All forms of ED result in progressive osteoarthritis, ultimately cumulating into degenerative joint disease (DJD).

Figure 1: Ununited Anconeal Process (UAP)
Figure 2: Fragmented Coronoid Process (FCP)
Figure 3: Osteochondrosis Dissecans (OCD)

2019 Cohort: 21 clinically normal Tollers from owners
2019: Elbow CT Photographs taken of each dog in standing position
Extract DNA from submitted samples
Genome Wide Association Study (GWAS)

2021: Release call to Toller owners and breeders for dogs diagnosed with ED with imaging
2021: receive imaging, ED status, and DNA samples of Tollers from call
Illumina Canine HD array genotyping 200,000 markers
Analyze images of 2019 cohort in photoshop

FCP Genome Wide Association Study Results

A genome wide association study (GWAS) was performed with 5 cases (only FCP phenotype) and 22 controls (non-FCP phenotype) NSDTR for a total of 25 dogs. Only dogs with robust CT imaging and phenotyping were included in our study. The GWAS was performed using Illumina HD SNP array. Genetic relatedness is shown in Figure 4.1 and population stratification is shown in Figure 4.2. The strongest association was on chromosome 9 but failed to reach Bonferroni significance.

The Effect of Chondrodystrophy on Height

After collecting phenotype data in photoshop as seen in Image 1, height measurement were compared to the number of copies of the chondrodystrophy (CDDY) retrogene in each genome (Figure 5). There is little difference between 0 and 1 copy of CDDY, however, 2 copies of CDDY has a significant effect on height \((P=0.027)\) when compared to 0 and 1 copies.

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References


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Conclusion

- Chromosome 9 (40-55 Mb) is a suspect region for FCP in NSDTR.
- SNPs on chromosome 9 (or any other chromosome) do not meet Bonferroni correction.
- AS expected, CDDY does have a significant effect on height and in this cohort appears to be dominant.

Future Directions

- More FCP cases with CT imaging and robust phenotyping are necessary to strengthen statistical power.