Investigations into the Genetic Origins of Orthopedic Phenotypes in the Novia 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.

Elbow Dysplasia

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).

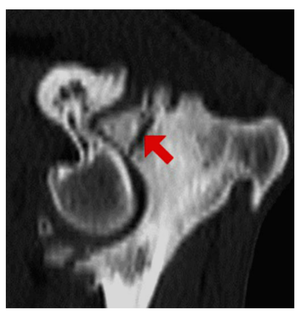


Figure 1: Ununited Anconeal Process (UAP)

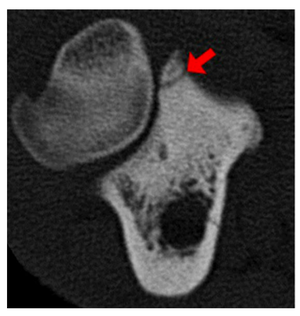


Figure 2: Fragmented Coronoid Process (FCP)

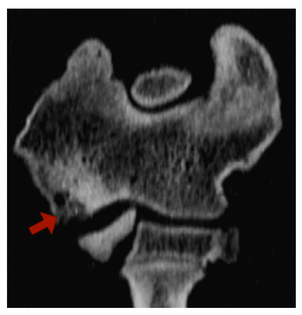
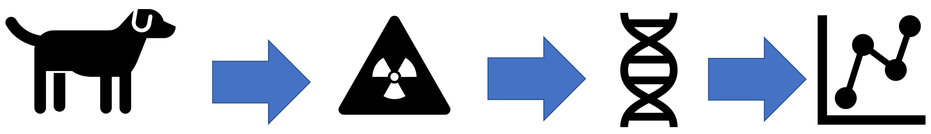


Figure 3: Osteochondrosis Dissecans (OCD)

Materials and Methods



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 preformed 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 preformed 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.

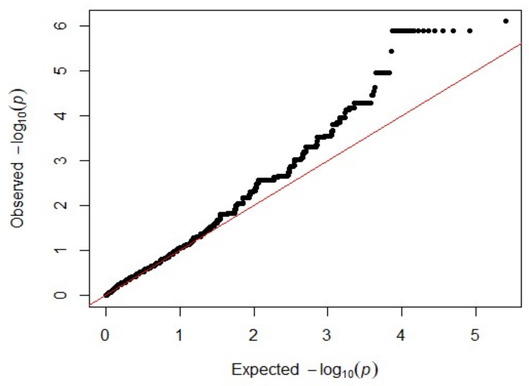


Figure 4.1

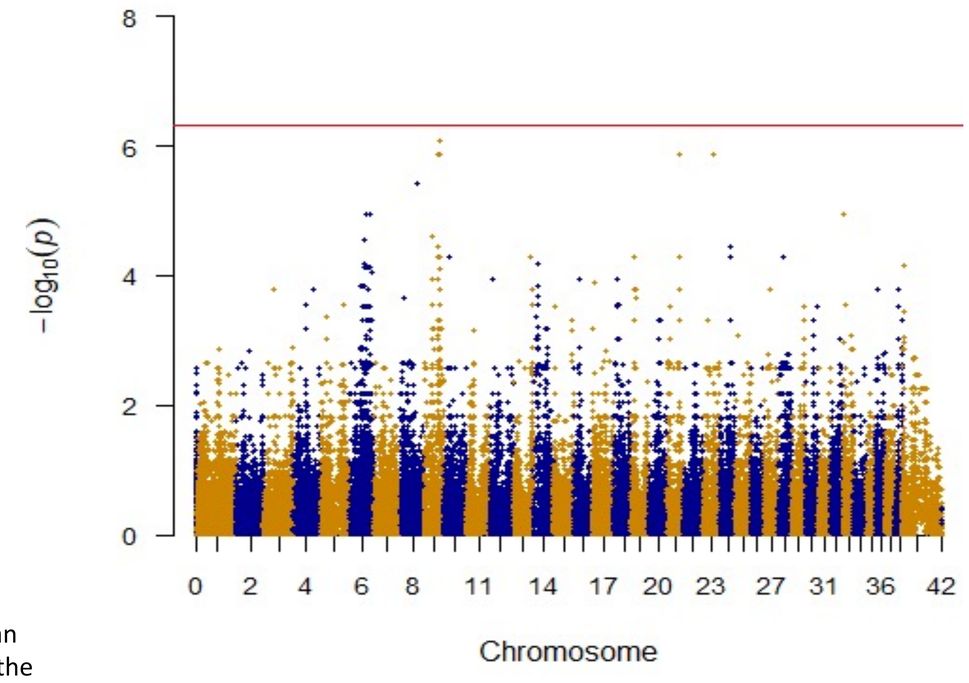


Figure 4.2

Figure 4.1: QQ plot of NSDTR sample set (n=25); lamda = 1.29. **Figure 4.2:** Manhattan plot of most associated alleles with FCP in the 25 NSDTR. Bonferroni significance shown as red line.

The Effect of Chondrodystrophy on Height

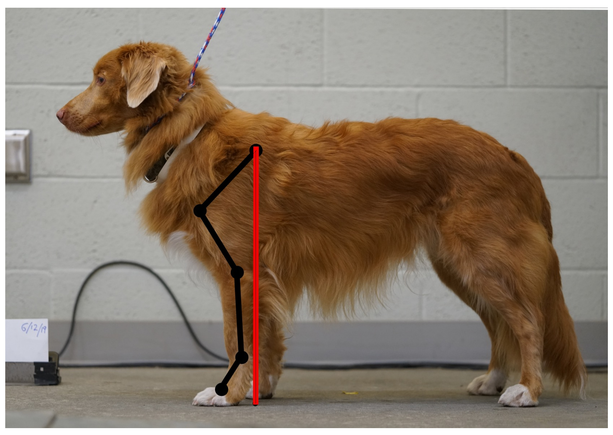


Image 1: NSDTR from 2019 chondrodystrophy CT study in standing position with joint angles (black lines) and height (red line) measured using photoshop.

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.

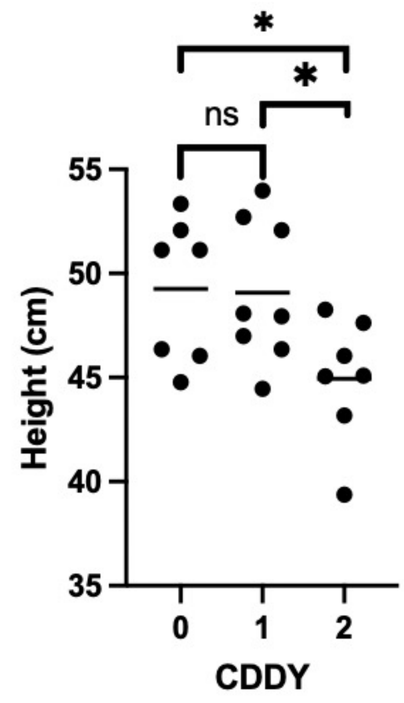


Figure 5: Height measurement phenotypes plotted against CDDY genotype status.

References

- Oberbauer AM, Keller GG, & Famula TR (2017) Long-term genetics election reduced prevalence of hip and elbow dysplasia in 60 dog breeds. PLoS ONE 12(2): e 0172918.
- Hayward JJ et al. (2016). Complex disease and phenotype mapping in the domestic dog. Nat. Commun. 7:10460 doi: 10.1038/ncomms10460

Conclusion

- Chromosome 9 (40-55 Mbp) 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.

Acknowledgments

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