# RESEARCH PROGRESS REPORT SUMMARY

**Grant 02400-MOU:** Basis of Dwarfism in Great Pyrenees

**Principal Investigator:** James Mickelson, PhD

**Research Institution:** University of Minnesota

**Grant Amount:** $18,745

**Start Date:** 1/1/2018 **End Date:** 6/30/2020

**Progress Report:** FINAL

**Report Due:** 6/30/2020 **Report Received:** 8/7/2020

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**Original Project Description:**

Great Pyrenees dwarfism is not fatal, but is a chondrodysplasia first scientifically described in the mid-1990s. Pups appeared normal at birth, but within two weeks were shorter and smaller than their non-dwarf littermates. This form of dwarfism is not due to hormonal imbalances. Pedigree analysis suggests that it is inherited in an autosomal recessive fashion, and is potentially caused by a single gene. Dogs suspected to be carriers for this condition have normal proportions. The specific underlying genetic cause and the true prevalence of this condition within the breed is unknown. The investigators hypothesize that dwarfism in Great Pyrenees dogs has a genetic basis in which whole genome scans with DNA markers can identify a small chromosomal region that will contain a dwarfism-associated gene, and that high-throughput DNA sequencing will identify the causative mutation(s). The goal is to determine the frequency of the DNA variant in the breed, and to develop and provide a genetic test to inform breeding decisions, and eventually aid in eradicating this disorder from the breed.

*Funding for the research is provided through the efforts and generosity of the Great Pyrenees Club of America. The AKC Canine Health Foundation supports the funding of this effort and will oversee grant administration and scientific progress reports.*

**Publications:** None at this time.

**Presentations:** None at this time.

**Report to Grant Sponsor from Investigator:**

Through the efforts of the Great Pyrenees community we were provided with sufficient samples from dwarf cases and related controls to perform a SNP marker whole genome scan to detect the position of a dwarfism gene. This produced a very significant localization of the dwarfism gene to a region of canine chromosome 33. Analysis of whole genome sequences from dwarf cases and controls did not identify any simple mutations in genes in the associated region on chromosome 33. However, when we focused on more complex sequence alterations in the region of interest on dwarf chromosome 33 we identified a structural rearrangement involving the insertion of the coding sequence of a gene whose complete sequence actually lies on chromosome 27. All dwarf cases carried two copies of the insertion and their parents are all carriers, consistent with recessive inheritance. Although the molecular mechanism by which the gene insertion causes dwarfism is not yet clear, the results have enabled a genetic test for carrier status and its use in predicting outcomes of breeding decisions.