



AMERICAN KENNEL CLUB
**CANINE HEALTH
FOUNDATION**
PREVENT TREAT & CURE

GRANT PROGRESS REPORT REVIEW

Grant: 01248: *Whole Genome Association Analyses for Cryptorchidism in Dogs*

Principal Investigator: Dr. Max F. Rothschild, PhD

Research Institution: Iowa State University

Grant Amount: \$74,104.00

Start Date: 1/1/2010 **End Date:** 12/31/2010

Progress Report: 12 month

Report Due: 12/31/2010 **Report Received:** 12/15/2010

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Background: Cryptorchidism, or retained testicles, is one of the common congenital problems in dogs. The testes of cryptorchids are more prone to testicular cancer and infertility. Therefore, cryptorchids and animals carrying genes for cryptorchidism should be eliminated from the breeding population. Some evidence exists to suggest that it appears to be a multigenic trait but single genes with large effects may exist. In earlier studies, the researchers utilized a candidate gene approach using 50 polymorphisms (called SNPs) in 22 candidate genes and found that collagen 2A1 (COL2A1) was significantly associated with cryptorchidism in Siberian Huskies. Now, they need to use the whole genome association analysis which typically provides more comprehensive analyses of chromosomal regions associated with a particular trait. This will then allow them to confirm previous findings or suggest other contributing regions or genes.

Objective: The researchers will utilize a new tool called the canine SNP chip which allows them to genotype for over 200,000 genetic differences between affected and unaffected animals. All results will be published and available freely to all dog breeders and they also aim to develop a test to remove the defect from the population.

Grant Objectives:

Objective 1: Genome wide SNP genotyping of cryptorchid cases and controls using the Illumina CanineHD BeadChip with more than 170,000 SNPs

Objective 2: Statistical analyses to discover SNPs associated with canine cryptorchidism

Objective 3: Provide recommendations for breeders based on the association results

Publications:

Report to Grant Sponsor from Investigator:

Cryptorchidism, or retained testicles, is one of the common congenital problems in dogs. The testes of cryptorchids are more prone to testicular cancer and infertility. Hence cryptorchids and animals carrying genes for cryptorchidism should be eliminated from the breeding population. Evidence exists to suggest that it appears to have a genetic cause. Therefore, the present study was performed to find the genetic differences on all chromosomes (genome wide) between 56 unrelated cryptorchid male dogs (cases) and 45 normal dogs (controls). More than 170,000 genetic differences called single nucleotide polymorphisms (SNPs) throughout the genome were tested between cases and controls using the Illumina CanineHD Genotyping BeadChip at GeneSeek, Lincoln, NE. Several advanced statistical methods were implemented to find the associated chromosomal regions and the genes within the regions for canine cryptorchidism. Our statistical association analyses for this defect indicated associated regions on chromosome 27 and chromosome 1. The associated region on chromosome 1 has a novel gene, whereas the associated region on chromosome 27 contained several genes including ATF1 (Activating transcription factor 1), DIP2B (DIP2 disco-interacting protein 2 homolog B), MTTL7A (Methyltransferase like 7A) and ACVR1B (Activin receptor1B). Some of these genes (DIP 2B and MTTL 7A) were thought to be involved in gene imprinting (their effect differs if they receive the gene from the mother or the father). However, we performed some genetic imprinting tests which then excluded obvious imprinting phenomenon. By using a few other statistical methods, we identified the predominant association of an interesting combination of three genetic differences on chromosome 27 with the cryptorchidism in Siberian Huskies. Hence the present results are very exciting, but further studies using additional animals from this breed are needed to confirm the present results and testing other breeds is needed to establish a genetic test for all canine cryptorchidism.