Name(s)

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Project Number

S1204

Project Title

Novel Insights into Human Obesity through Identification of Genetic Polymorphisms in Lean vs. Obese Labrador Retrievers

Abstract

Objectives

Mutations in the proopiomelanocortin (POMC) gene have been associated with obesity in Labrador retrievers while mutations in the related melanocortin-4 receptor (MC4R) gene have been associated with obesity in humans. We hypothesize that polymorphisms exist in the POMC, MC4R and nearby genes between an obese and a lean Labrador retriever and that studying these genetic variants may lend insight into obesity.

Methods

DNA obtained from an obese and a lean Labrador was run on a microarray chip containing over 200,000 genetic markers (Embarkvet). The UCSC browser Canine 3 genome assembly was used to analyze the data.

Results

The dogs have different genotypes at all of the markers within the POMC and MC4R genes. While interrogating the POMC gene we encountered several variants at the adjacent NCOA1 gene. The dogs have different genotypes at five of the 6 markers in NCOA1. Interestingly, the obese dog is homozygous for the wild type alleles in the POMC and NCOA1 genes while the lean dog has the polymorphisms. The lean dog is homozygous for the wild type allele in the MC4R gene while the obese dog has the polymorphism. These genes are implicated in energy intake and expenditure, and the dogs have measurable differences in these indices.

Conclusions

This research provides insights into the genetic basis for and linkages between canine and human obesity, and offers a roadmap for using comparative genomics as a translational tool for studying high impact human diseases, such as obesity.

Summary Statement

Polymorphisms in the POMC, MCR-4, and NCOA1 genes exist in Labrador Retrievers and may lend insight into human obesity.

Help Received

Barbara Natterson-Horowitz MD, Sara Makanani, Karol Watson MD PHD, Jessica Wang MD PHD, University of California Santa Cruz open source genome browser