New dwarfism mutation identified in dogs

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Professor Hannes Lohi's research group at the University of Helsinki and Folkhälsan Research Center has identified a mutation in ITGA10 gene, causing chondrodysplasia in two dog breeds, the Norwegian Elkhound and the Karelian Bear Dog. The research revealed a new chondrodysplasia gene in dogs, and a candidate gene for human chondrodysplasias. The finding has implications on bone biology as well as canine health. A genetic test can now be used to identify mutation carriers in the two affected dog breeds. The study was published on the scientific journal *PLOS ONE* on 25 September 2013.

The ITGA10 mutation causes autosomal recessive disproportionate short-stature dwarfism of varying severity. The appearance of affected dogs is characterized considerably shorter limbs than normal dogs, and other skeletal abnormalities may follow, including bowed forearms, abnormal digits, and malformed femoral heads.

The ITGA10 gene codes for an integrin subunit that assembles into a cartilage-specific collagen receptor, found in the growth plates of long bones. The receptor is important for the process of endochondral ossification, in which the cartilage cells first proliferate, and are then replaced by bone tissue. Accordingly, several abnormalities have been found in the growth plates of affected dogs both in radiographic and histological examinations.

Collagen-receptor mutation causes growth disturbances

The causative mutation was mapped to a specific region on canine chromosome 17 by comparing the genomes of affected and healthy dogs. Further analysis of this chromosomal region revealed a single nucleotide change in the ITGA10 gene, which disrupts the gene by introducing signal that prematurely ends the production of the encoded integrin subunit. "Because of the premature stop codon, the full length integrin subunit is never made, and consequently, there are no functional receptors in the affected dogs' growth plates. This causes the growth disturbances", explains Professor Lohi, and continues: "Several collagen mutations have been previously found in different growth disorders but this is only the second collagen receptor that has been linked to inherited chondrodysplasia. Our canine disease model offers new possibilities to study growth plate biology".

The results of the study may have implications to human medicine as well. "Humans also suffer from different types of inherited chondrodysplasia, and the ITGA10 gene could represent a good candidate gene for some of these disorders, which still have an unknown genetic cause", tells Kaisa Kyöstilä, the first author of the paper. "We have already begun screening human patients for mutations in the gene", she adds.

A gene test recognizes mutation carrier dogs

The studied canine chondrodysplasia was initially described in Norwegian Elkhounds in the 1980's, and the current study identifies a corresponding problem in Karelian Bear Dogs. "Both breeds have now benefited from a genetic test that is available for dog owners", tells Professor Lohi. "The test is used to recognize mutation carriers, and the long-term aim is to eradicate the mutation and the disease from the dog breeds", he concludes.

The research group led by Professor Lohi is based at the Faculties of

Veterinary Medicine and Medicine in the University of Helsinki and at the Folkhälsan Research Center. Professor Lohi's research has been supported by the University of Helsinki, the Academy of Finland, the Sigrid Juselius Foundation, Biocentrum Helsinki, the Jane and Aatos Erkko Foundation, and Folkhälsan.

More information: Kyöstilä K, Lappalainen AK, Lohi H. Canine Chondrodysplasia Caused by a Truncating Mutation in Collagen-binding Integrin Alpha Subunit 10. (2013) *PLOS ONE*, dx.plos.org/10.1371/journal.pone.0075621

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