New insights into human rare disorders with dogs

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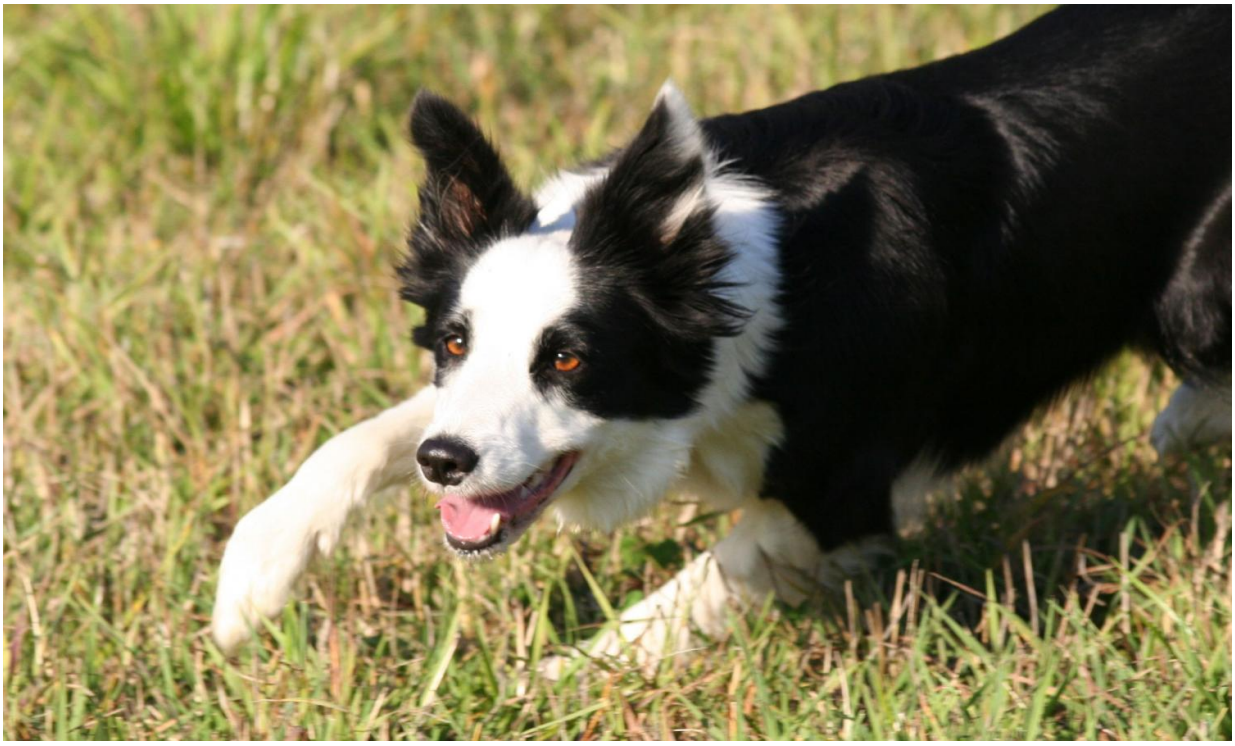

Genetic research in dogs revealed the causes of hyperostosis in Terrier breeds, dental hypomineralization in Border Collie, and previously undescribed skeletal syndrome in Wire Fox Terriers. Credit: Marjo Hytönen

Professor Hannes Lohi's research group at the University of Helsinki has discovered three novel canine genes for Caffey, Raine and van den Ende-Gupta syndromes. Research reveals close similarities of the canine

models of human rare disorders and highlights the potential of comparative research approach for the development of rare disease diagnostics and treatments. Gene discoveries will benefit also veterinary diagnostics and breeding programs. The study was published in *PLOS Genetics* on May 17, 2016.

Genetic research in dogs revealed the causes of hyperostosis in Terrier breeds, dental hypomineralization in Border Collie, and previously undescribed skeletal syndrome in Wire Fox Terriers. The latter two syndromes were described first time in the study. Hyperostosis in Terriers have been described before but the genetic cause was found here. Gene discoveries helped to identify and name the conditions and link them to human rare disorders.

New candidate gene to human Caffey disease

The study unraveled a novel candidate gene for human Caffey disease, a condition that causes facial swelling and other symptoms. Gene discovery for canine craniomandibular osteopathy (CMO) is of particular interest. The disease is known as infantile hyperostosis in human and belongs to a group of self-limiting and difficult to diagnose swelling syndromes. We found a novel physiologically relevant candidate gene, SLC37A2, and have initiated mutation screenings in human Caffey patients explains lead author, PhD Marjo Hytönen. SLC37A2 is a glucose-phosphate transporter, and its defect suggests an impaired glucose homeostasis in developing bone, leading to hyperostosis. New canine model provides resources to better understand SLC37A2 functions in skeletal biology.

Gene discovery necessary for disease diagnostics

This study provides molecular identity for the canine conditions.

Mutations in the SCARF2 and FAM20C genes have been associated with the human van den Ende-Gupta and Raine syndromes. Van den Ende-Gupta syndrome is characterized by a heterogeneous variety of craniofacial and skeletal abnormalities, and Raine syndrome by hypomineralization of bones and teeth. The clinical features in canine models closely resembled human syndromes. These two examples demonstrate again how similar human and canine rare disorders are clinically and genetically. This is important since many of these developmental disorders cannot be efficiently replicated in mouse models. Dogs are large animals with more similar physiology and therefore better models. There is a growing interest in the development of better diagnostic and treatment options for rare disorders, and canine models can reveal genes and provide resources to better understand the conditions and even to try new treatments. Comparative studies in rare disorders between humans and dogs should be increased in future, comments professor Hannes Lohi, the corresponding author.

Three new genetic tests for diagnostics and breeding

The study has also practical implications for veterinary diagnostics and breeding programs to improve canine welfare. Genetic tests developed in this study will help veterinarians to diagnose the conditions, which is often challenging in the developmental syndromes based on only clinical characteristics. Gene tests will also improve breeding programs since breeders have now new tools to identify carriers and to select proper mating partners to avoid affected puppies in future litters, explains Marjo Hytönen. The three gene tests can be found from MyDogDNA-gene panel test.

The research group led by Professor Lohi is based at the Veterinary and Medical Faculties in the University of Helsinki and at the Folkhälsan Research Center.

Provided by University of Helsinki