

# Study finds same genes behind heart muscle disorders in humans and Dobermanns

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Researchers from the University of Helsinki and the Folkhälsan Research Center, together with their international partners, have identified the genetic background of dilated cardiomyopathy, a disease

that enlarges the heart muscle, in dogs and humans. The findings are published in the journal *Genome Medicine*.

Based on a dataset encompassing more than 500 Dobermanns, the [disease](#) was associated with two nearby genomic loci, where changes were identified in [genes](#) that affect the functioning, energy metabolism and structure of the heart muscle. The study revealed that these same risk genes cause [heart muscle disease](#) in human patients.

A variety of factors can cause [cardiomyopathy](#), but genetics play a significant role. Although dozens of genes underlying cardiomyopathy in humans have been identified, the hereditary nature and genetic background of the disease in dogs have remained unclear.

"The situation with Dobermanns is serious in terms of both their health and breeding. The disease has been studied from various angles for decades without significant gene discoveries. Better diagnostic tools are needed, particularly in early diagnostics. Our new research might improve the situation," says Professor Hannes Lohi, the principal investigator in the project.

The study has significant implications for [veterinary medicine](#), providing a basis for developing a new genetic test for early diagnostics and breeding.

## **Two novel risk genes identified in an extensive European cohort**

Various research data collected over decades on more than 500 Dobermanns from across Europe were combined for the research. The dogs in the study cohort were categorized into five different groups:

- Dogs with only dilated cardiomyopathy
- Dogs with only arrhythmia
- Dogs with dilated cardiomyopathy and arrhythmia
- Dogs with congestive heart failure
- Healthy dogs aged at least six years as a control subcohort

With the help of genetic mapping, two adjacent gene loci in chromosome 5 were associated with dilated cardiomyopathy. Among the numerous genes in the loci, two, namely RNF207 and PRKAA2, demonstrated structural variation, which could have a detrimental effect on the functioning of the genes and cause heart failure.

"The genetic mapping we conducted produced important observations. Until now, it has been unclear whether Dobermanns with differing symptoms have the same disease. The genes we identified are only associated with a dilated [heart](#) and affected cardiac function. Arrhythmia appears to be a genetically distinct disease. Our dataset was insufficient to identify genes causing arrhythmia only. We also observed that several genes affect cardiac function and identified a model of two genes that increase the disease risk," explains Professor Lohi.

## **Gene discovery in dogs associated with cardiac muscle disorders in humans**

The significance of the gene discovery in dogs was investigated in [human patients](#) diagnosed with dilated cardiomyopathy using Dutch, English (UK Biobank) and Finnish (FinnGen) cohorts. Fifteen potentially harmful and predisposing variants in the same RNF207 and PRKAA2 genes, which had been identified in dogs, were discovered in humans.

"The identical [genetic background](#) suggests that, to a degree, similar

problems with the functioning of the [heart muscle](#) lead to dilated cardiomyopathy in both humans and dogs. A deeper understanding of the pathogenetic mechanisms is important, and Dobermanns represent a natural model organism for further research," Lohi states.

## A genetic test for breeding

The DNA markers associated with the disease found in the study may be a step toward a genetic test, but it is important to confirm its clinical significance before such tests are offered.

"We discovered how the variants of the two genes together increase the disease risk. However, a pilot is needed to combine genetic and health data to monitor how frequently individuals who belong to the at-risk group develop the disease for varying genetic reasons. Then, we can obtain a more accurate estimate of how the gene discoveries should be ideally interpreted and utilized. In any case, this is a hope-inspiring finding because, in the past, we lacked such tools," Lohi describes.

**More information:** Julia E. Niskanen et al, Identification of novel genetic risk factors of dilated cardiomyopathy: from canine to human, *Genome Medicine* (2023). [DOI: 10.1186/s13073-023-01221-3](https://doi.org/10.1186/s13073-023-01221-3)

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