New PRA gene identified in Phalenes and Papillons

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Papillon dog. Credit: Kaisa Kuutti

Finnish researchers have identified a genetic mutation causing progressive retinal atrophy (PRA) in the Phalene and Papillon dog breeds. PRA is one of the most common causes of blindness in dogs and

in human. This study highlights the shared genetic etiology of many canine and human genetic disorders, and provides new tools to investigate PRA mechanisms while the beloved dogs benefit from genetic testing.

Professor Hannes Lohi's research group at the University of Helsinki and Folkhälsan Research Center, Finland, has identified a mutation in CNGB1 gene, causing progressive retinal atrophy (PRA) in the Phalene and Papillon dog breeds. PRA is one of the most common causes of blindness in dogs and in human. CNGB1 mutations have been previously associated with the corresponding human disease, human retinitis pigmentosa. This study highlights the shared genetic etiology of many canine and human genetic disorders, and provides new tools to investigate PRA mechanisms while the beloved dogs benefit from genetic testing. The study was published in the scientific journal *PLOS ONE* on August 28, 2013.

Progressive retinal atrophies are common causes of blindness in human and dogs. PRA is caused by the degeneration of the photoreceptor cells, rods and cones, which are needed for dark and day light vision, respectively. PRA often progresses in stages from impaired dark vision to complete blindness. Typical retinal changes are visible in eye examination usually around 3 years of age. There are already 12 known PRA genes found in dogs.

Phalenes and Papillons have mutation in the same gene as human PRA patients

This study aimed to discover the genetic cause of PRA in the Phalene and Papillon breeds. Gene discovery was accomplished by only six PRA-affected dogs.

"Most PRAs, including the one in Phalenes and Papillons, are recessive and caused by single gene defects and small sample numbers can lead to breakthroughs. The symptoms in Phalenes and Papillons start at 5 years of age, and we found some younger genetically affected dogs, who are likely to get PRA later and should be carefully followed," explains corresponding author, professor Hannes Lohi.

New technology facilitates gene discovery

The new CNGB1 mutation in Phalenes and Papillons was discovered with six cases and 14 control dogs and confirmed in a larger cohort of dogs. Gene discovery was greatly facilitated by a new exome sequencing technology, which analyzes all protein-coding regions of the genome at once.

"The rapid advancement of gene technology greatly facilitates gene discovery. After gene mapping we had several candidate regions to choose but exome sequencing quickly identified the actual mutation. The same technology opens possibilities with many other eye conditions we are currently working on," explains lead author Saija Ahonen.

The mutation in Phalene and Papillon dogs was found in the gene, which has been linked to corresponding human retinal degeneration earlier.

"This research demonstrated again the shared disease heritage between dogs and humans. The same genes are often affected in the same diseases in both species. This is advantageous, since dogs provide new models to investigate the disease mechanisms and to plan new therapies such as gene therapy, successfully applied to blindness in dogs and human previously," explains Lohi.

Gene testing helps breeding plans

The identified mutation in the CNGB1 gene prevents the generation of normal protein in the dog's eyes. This protein is needed in the rod cells to maintain dark vision, and the absence of the protein leads to impaired dark vision in Phalenes and Papillons.

"We tested the mutation in altogether 500 dogs in different breeds. It seems to be present only in Phalenes and Papillons and nearly every fifth (20%) dog carries the mutation. Gene test is indeed needed since it is not recommended to breed to carriers to avoid affected puppies. At the same time, veterinarians and breeders can use the gene test as a diagnostic tool," explains Ahonen. This study is part of her upcoming PhD thesis.

More information: Saija, A. et al. A CNGB1 Frameshift Mutation in Papillon ja Phalene Dogs with Progressive Retinal Atrophy, *PLOS ONE*, 2013. dx.plos.org/10.1371/journal.pone.0072122

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