

Genetic risk factor for laryngeal paralysis in miniature bull terriers identified

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Nugget, a six-year-old Miniature Bull Terrier with permanent tracheostomy due to life-threatening laryngeal paralysis. Credit: Dr. Birgit Hagen

Laryngeal paralysis is a serious and sometimes deadly disease in some dog breeds that prevents proper opening of the larynx for breathing. In a new study published 24th October in *PLOS Genetics*, a team of German specialists in canine head and neck surgery and geneticists from the University of Bern identify a mutation responsible for laryngeal paralysis in Miniature Bull Terriers, enabling the development of a genetic test for the disease.

Laryngeal paralysis most commonly affects middle-aged or geriatric dogs belonging to large and giant dog breeds, but recently breeders observed a rise in laryngeal paralysis striking in young Miniature Bull Terriers. To identify a [genetic cause](#), researchers performed a [genome-wide association study](#) and analyzed genome sequences of several hundred dogs to find mutations that occur in Miniature Bull Terriers with the disease. In the genome of affected dogs, they discovered an extra piece of DNA inserted into the RAPGEF6 gene that results in production of an incomplete, nonfunctional RAPGEF6 protein. Miniature Bull

Terriers that carried only mutant versions of the gene had a 10- to 17-fold increased risk of laryngeal paralysis.

The researchers did not detect a perfect correlation between the mutation and the laryngeal paralysis, which suggests that other genetic and environmental factors also may contribute to the development of the disease. Additionally, this mutation only occurred in Miniature and standard Bull Terriers, and thus cannot explain laryngeal paralysis in other [dog breeds](#). However, the study identifies an important role for RAPGEF6 in laryngeal nerve function.

The authors emphasize the important contribution of concerned dog owners in initiating this research: "We are very excited about this breakthrough in research that has been made possible by a fantastic effort of many highly motivated dog breeders and owners who alerted us to the problem and donated samples from their dogs," commented senior author Tosso Leeb. "Targeted breeding should drastically reduce the frequency of this devastating disease in the future."

With this information, a genetic test for the mutation can now be developed to prevent the breeding of Miniature Bull Terriers and Bull Terriers that are at risk for the disease.

More information: Hadji Rasouliha S, Barrientos L, Anderegg L, Klesty C, Lorenz J, Chevallier L, et al. (2019) A RAPGEF6 variant constitutes a major risk factor for laryngeal paralysis in dogs. *PLoS Genet* 15(10): e1008416. doi.org/10.1371/journal.pgen.1008416

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