A new model of centronuclear myopathy in Great Danes


History of the disease

Few years ago, cases of inherited myopathy in Great Danes living in Canada and Australia have been reported by two independent scientific groups¹. These initial cases were described as "Central core myopathy” or “Inherited Myopathy of Great Danes” and movies of affected dogs can be seen on www.centralcoremyopathy.info/video.htm.

Histopathological and molecular characterization of the disease

More recently, additional cases have been diagnosed in the USA and in-depth evaluation of muscle biopsies revealed that this autosomal recessive disorder has indeed histological features of centronuclear myopathy (CNM), and more precisely of a highly progressive human forms of CNM that remained unresolved at the molecular level. Common histopathological features between human and canine forms are displayed on the following figure, with centralized nuclei (arrows) and membrane defects (arrow heads).
Our scientific work then consisted in identifying the genetic mutation causing CNM in Great Danes. A mutation in the *BIN1* gene, previously implicated in autosomal recessive centronuclear myopathy in human\(^2\), was found to be the cause of this canine myopathy.

In dogs, careful analyses of pedigrees including affected dogs (probands, see an example below, excerpted from the manuscript) allowed to postulate that a unique mutation accounts for all cases of this specific inherited myopathy described recently in the USA and previously in the UK, Canada and Australia.

A direct consequence of this molecular characterization is the development of a genetic test for CNM in Great Danes, meaning that owners now have the possibility to confirm at the DNA level which of disabled dogs are indeed affected by this form of CNM as previously performed in Labrador retrievers\(^3\) (www.labradorcnm.com), to avoid matings at risk in the future, and to identify carrier for the establishment of a colony for research use.

Importantly, a similar mutation of the same *BIN1* gene was also found in human patients, with highly similar muscle alterations and phenotypes. This canine model impressively mimics a highly progressive autosomal recessive form of centronuclear myopathy in humans.

