

# Genetics of Canine Primary Glaucomas

András M. Komáromy, DrMedVet, PhD<sup>\*</sup>, Simon M. Petersen-Jones, DVetMed, PhD

## KEYWORDS

• *ADAMTS10* • *ADAMTS17* • Canine • Genetics • Glaucoma • Open-angle  
• Closed-angle • Lens luxation

## KEY POINTS

- Primary angle-closure glaucoma (PACG) is the most common form of canine primary glaucoma and is a complex trait with multiple genetic and possibly environmental risk factors.
- Five susceptibility genes or loci have been identified as possible contributors to canine PACG.
- Primary open-angle glaucoma (POAG) is a monogenic, autosomal-recessively inherited disease, and it has recently been associated with primary lens luxation (PLL).
- Discoveries of disease mutations in *ADAMTS10* and *ADAMTS17* suggest that canine POAG and PLL are homologous to the human connective tissue disorders Weill-Marchesani and Marfan syndromes.
- Identification of canine glaucoma disease genes and development of genetic tests will help to avoid the breeding of affected dogs and enable earlier diagnosis and potentially more effective therapy.

## INTRODUCTION

Glaucoma is a leading cause of incurable vision loss in dogs.<sup>1,2</sup> It is defined as an optic neuropathy with characteristic damage of the optic nerve head, retinal ganglion cell death, and resulting loss of sight.<sup>3</sup> In most affected dogs, abnormal intraocular pressure (IOP) elevation leads to degeneration of the optic nerve and retina.<sup>3</sup> Compared with healthy eyes, in which physiologic IOP is maintained by a tight regulation of aqueous humor production and drainage, in glaucomatous eyes the outflow of

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<sup>\*</sup> Corresponding author.

E-mail address: [komaromy@cvm.msu.edu](mailto:komaromy@cvm.msu.edu)

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aqueous humor through the iridocorneal angle (ICA) is impaired, resulting in an IOP increase.<sup>4,5</sup> In primary glaucomas, both eyes are typically affected by an increased resistance along the aqueous outflow pathways, resulting from primary abnormalities, rather than secondary to other pathologic intraocular processes, as in secondary glaucoma.<sup>1,3</sup> Based on the specific breed predilection for primary glaucomas, genetic factors are suspected to be major contributors to the cellular and molecular disease mechanisms resulting in impaired aqueous humor outflow.<sup>1</sup> Both the American and European Colleges of Veterinary Ophthalmologists recommend against the breeding of dogs affected by primary glaucomas (Table 1).<sup>6,7</sup> Despite the high prevalence of primary glaucomas in dogs,<sup>1</sup> their genetics has been studied in only a relatively small number of breeds. This review serves as a comprehensive summary of the current knowledge of the genetics of primary glaucomas in dogs. Because of their close association with either primary angle-closure glaucoma (PACG) or primary open-angle glaucoma (POAG),<sup>8–13</sup> the genetics of pectinate ligament dysplasia (PLD) and primary lens luxation (PLL) are also discussed. Recent advances in the genetics of canine glaucomas have provided a better understanding of molecular and cellular

**Table 1**

**Breeds affected by primary glaucomas or primary lens luxation according to the American College of Veterinary Ophthalmologists and the European College of Veterinary Ophthalmologists**

<b>Primary Glaucoma</b>	<b>Primary Lens Luxation</b>
Alaskan malamute	Australian cattle dog <sup>a</sup>
American cocker spaniel	Border collie
Australian cattle dog <sup>a</sup>	Brittany
Basset hound (PLD)	Brussels griffon
Beagle	Bull terrier
Boston terrier	Chinese crested dog
Bouvier des Flandres (PLD)	Chinese shar-pei <sup>a</sup>
Bullmastiff	Greyhound
Chinese shar-pei <sup>a</sup>	Italian greyhound
Chow Chow	Jack Russell terrier <sup>a</sup>
Dalmatian	Lancashire heeler
English cocker spaniel	Miniature bull terrier
English springer spaniel	Parson Russell terrier
Entlebucher	Petit basset griffon vendéen <sup>a</sup>
Eurasier	Pyrenean shepherd
Flat-coated retriever (PLD)	Rat terrier
Golden retriever	Sealyham terrier
Great Dane	Smooth fox terrier <sup>a</sup>
Jack Russell terrier (PLD) <sup>a</sup>	Spanish water dog
Labrador retriever	Tibetan terrier
Newfoundland (PLD)	Toy fox terrier
Norwegian elkhound	Welsh terrier <sup>a</sup>
Petit basset griffon vendéen <sup>a</sup>	Wire fox terrier <sup>a</sup>
Poodle (PLD)	Yorkshire terrier
Samoyed	
Shiba inu (PLD)	
Siberian husky	
Smooth fox terrier <sup>a</sup>	
Welsh springer spaniel (PLD)	
Welsh terrier <sup>a</sup>	
Wire fox terrier <sup>a</sup>	

<sup>a</sup> Breeds affected by both primary glaucomas and PLL.

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