

Implications of the LPN1 Mutation for Breeding

Letter Key:

N = Normal copy of the LPN1 gene

D = Mutated copy of the LPN1 gene

Breeding two clear dogs

		Sire's Genotype	
		N	N
Dam's Genotype	N	N/N	N/N
	N	N/N	N/N

Breeding a clear dog to an affected dog

		Sire's Genotype	
		N	N
Dam's Genotype	D	D/N	D/N
	D	D/N	D/N

Breeding a clear dog to an at risk dog

		Sire's Genotype	
		N	N
Dam's Genotype	N	N/N	N/N
	D	D/N	D/N

Breeding an at risk dog to an affected dog

		Sire's Genotype	
		N	D
Dam's Genotype	D	D/N	D/D
	D	D/N	D/D

Breeding two at risk dogs

		Sire's Genotype	
		N	D
Dam's Genotype	N	N/N	D/N
	D	D/N	D/D

Breeding two affected dogs

		Sire's Genotype	
		D	D
Dam's Genotype	D	D/D	D/D
	D	D/D	D/D

One way to present the probability that puppies with severe, early-onset LPN1 will be produced from the mating of parents of each of the three possible genotypes is shown above. Each parent, depending on its genotype, will contribute either the D (mutated) or the N (normal) form of the LPN1 gene to a puppy. This in turn will result in that particular puppy's own genotype of N/N, D/N, or D/D. Each of the four outcome squares shown for each of the six possible matings in the above figure represents a 25% chance for producing a pup with that genotype. Thus, the matings resulting in one, two or four red squares will **on average** produce litters containing 25%, 50% and 100% severe, early-onset affected pups, respectively.

Our current data suggests that LPN1 is most likely inherited in a dominant, dose-dependent fashion (more copies of the LPN1 mutation = more severe disease), although other models of inheritance are still possible. D/N dogs are at risk for developing LPN1, though typically

clinical signs are milder, and the age of onset is later than is seen in D/D (affected) dogs. For example, breeding a D/N sire to an N/N dam can only produce puppies that are D/N or N/N (2 blue squares and 2 purple squares), and according to available data, no pups with the severe, early-onset form of LPN1 would be produced. On the other hand, breeding a D/N sire to a D/D dam gives a 50% chance that a puppy will have severe, early-onset LPN1 since puppies can be either D/N or D/D (2 purple squares and 2 red squares). All puppies from the mating of two D/D parents will be D/D and susceptible to the severe, early-set form of LPN1 (four red squares). Mating a D/D parent to a clear N/N parent would not produce affected early-onset puppies due to LPN1 (four purple squares), but all would be D/N (currently considered at risk for LPN1).

Lastly, and very importantly, we do not recommend selecting dogs for breeding based solely on their both being N/N for the LPN1 gene. Such a drastic strategy, although more quickly eliminating the possibility of producing D/D genotypes and LPN1 affected dogs, also has the undesired effects of constricting an already small breeding pool, and losing many of the outstanding traits expected of Leonbergers. A better approach would enable the continued use of some of the many excellent D/N dogs by mating them to N/N dogs. This would produce litters of only D/N or N/N puppies, and none with the severe, early-onset form of LPN1, giving a choice of dogs to use for future breeding. By mating desirable D/N dogs to N/N dogs, the frequency of the D form of the LPN1 gene can be progressively decreased.