SHAR-PEI AUTOINFLAMMATORY DISEASE (SPAID) TEST

Shar-Pei Autoinflammatory Disease (SPAID) is a heritable syndrome defined by recurrent episodes of fever and inflammation with no known pathogenic or autoimmune cause. SPAID is characterised by five signs of inflammation, Familial Shar-Pei Fever (FSF), Arthritis, Vesicular Hyaluronosis, Otitis and Amyloidosis.

The SPAID Test identifies Shar-Pei most likely to be affected by SPAID during their lifetime. The result can be used by owners two-fold: i) as a health tool to suggest a dog should be watched more carefully for signs of SPAID and ii) as a breeding tool with the aim of reducing the presence of SPAID in the worldwide Shar-Pei population.

GROUP	SPAID TEST RESULT	OUTCOME	EXPLANATION
NON CARRIER	CNV = 2 Alleles = 1 & 1	Not expected to suffer SPAID	• The dog does not carry the variant associated with SPAID (i.e. allele 5). • The dog has no increased risk of disease.
SINGLE CARRIER	CNV = 6 Alleles = 1 & 5	Potential to suffer SPAID	• The dog carries one copy of the variant associated with SPAID (i.e. allele 5). • This dog is four times more likely to suffer SPAID than a non-carrier. • If bred with another Single Carrier, there is a 25% chance that a Double Carrier will result from the mating.
DOUBLE CARRIER	CNV = 10 Alleles = 5 & 5	Most likely to suffer SPAID	• The dog carries two copies of the allele associated with SPAID (i.e. allele 5). • This dog is eight times more likely to suffer SPAID than a non-carrier and is likely to suffer SPAID during their lifetime.

A HERITABLE DISEASE LINKED TO THE DISTINCTIVE APPEARANCE OF SHAR-PEI

It has been shown that the genetic variant linked to SPAID is also associated with the increased expression of Hyaluronan Synthase 2 (*HAS2*), the driver of long-chain hyaluronan (HA) synthesis. The elevated expression of *HAS2* results in hereditary cutaneous hyaluronanosis, and the breed's heavily thickened and wrinkled skin.

It is hypothesized that the recurrent inflammation experienced by some Shar-Pei is an effect of the over production and subsequent degradation of abundant high molecular weight HA, via natural homeostasis and other numerous environmental factors. The resultant low molecular weight HA acts as a danger associated molecular pattern "DAMP" and triggers the release of inflammatory interleukins.

Shar-Pei Autoinflammatory Disease (SPAID) encompasses multiple signs of inflammation. The clinical disease status of a dog is a product of the genetic marker tested here and the effect of the dog's environment. This is the only available test for SPAID. The results of this test cannot exclude that the dog assayed carries other mutations that can cause inflammatory disease in Shar-Pei.

ASSOCIATED PUBLICATIONS

- Olsson M et al. 2016. Absolute quantification reveals the stable transmission of a high copy number variant linked to autoinflammatory disease. BMC Genomics. 17(1):299.
- Olsson M et al. 2013. Thorough investigation of a canine autoinflammatory disease (AID) confirms one main risk locus and suggests a modifier locus for amyloidosis. PLoS One. 8(10):e75242.
- Olsson M et al. 2011. A novel unstable duplication upstream of HAS2 predisposes to a breed-defining skin phenotype and a periodic fever syndrome in Chinese Shar-Pei dogs. PLoS Genet. 7(3):e1001332.