A Genetic Comparison of Standard and Miniature Poodles based on autosomal markers and DLA class II haplotypes.

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It is widely assumed that Toy, Miniature and Standard Poodles are one breed differing only by their shoulder height. Miniature Poodles are also relatively free of the autoimmune disorders that affect Standard Poodles, such as Addison's disease, sebaceous adenitis, and chronic active hepatitis. This difference makes Miniature Poodles a possible source of genetic diversity free of these disorders. Thus, some breeders advocate cross-breeding Miniature Poodles with Standard Poodles as a means to increase genetic diversity of Standard Poodles and reduce the prevalence of these autoimmune disorders. There is also evidence that the both SA and Addison's disease are complex genetic traits with incomplete heritability, and that the genetic susceptibility to these diseases is fixed in Standard Poodles. If this is so, there is no way to do a case and control comparison to identify genetic associations for these diseases. If Miniature Poodles are closely related to Standard Poodles, they may serve as controls for a control vs. case comparison for SA and Addison's disease. However, if Miniature Poodles are genetically distinct from Standard Poodles, they would not prove useful for such a study. It would be extremely difficult to discern which genetic differences are due to traits that confer the Miniature and Standard Poodle phenotypes and genetic differences that are associated with SA or Addison's disease.

In the following study, we compared the genetic makeup of Miniature and Standard Poodles by using 24 single tandem repeat (STR) markers over 20 of the 38 canine autosomes, as well as by comparing DLA class II haplotypes and relative haplotype frequency. Table 1 shows the *F* statistics for four populations of dogs – SA affected and healthy Standard Poodles, Miniature Poodles and show English Setters. Show English Setters were included to demonstrate how a distinctly different breed might look next to Poodles. Standard Poodles, whether healthy or SA affected, are not distinguishable from each other with the exception of a somewhat lower average number of alleles utilized at each STR loci (indicating that SA affected Standard Poodles are somewhat more inbred than healthy dogs). Miniature Poodles are more genetically heterogeneous than Standard Poodles in terms of the average and effective number of alleles at each STR loci, observed heterozygosity and ultimate heterozygosity, while show English Setters are the least genetically diverse of the four populations by all parameters.

Table 1- Genetic comparison of four populations of dogs based on allele frequencies at 24 STR loci on 20 different chromosomes – 1) Standard Poodles suffering from sebaceous adenitis (SP-SA), 2) Healthy Standared Poodles (Sp-Control), 3) Miniature Poodles (Mini-Poodle), and 4) show English Setters (Eng-Show). F Statistics include average number of alleles utilized (Na), number of effective alleles (Ne), observed (Ho) and expected heterozygosity (He), ultimate heterozygosity (UHe), and coefficient of inbreeding (F).

Mean and standard error (SE) over Loci for each Population									
Population		N	Na	Ne	I	Ho	He	UHe	F
Pop1	Mean	33.565	5.087	2.900	1.170	0.566	0.610	0.619	0.078
SP-SA	SE	0.123	0.266	0.198	0.070	0.036	0.032	0.033	0.029
Pop2	Mean	67.304	6.217	2.925	1.215	0.593	0.619	0.623	0.050
SP-CONTROL	SE	0.213	0.361	0.196	0.063	0.033	0.028	0.029	0.021
Pop3	Mean	48.870	6.043	3.505	1.384	0.635	0.690	0.697	0.080
MINI-POODLE	SE	0.095	0.369	0.234	0.059	0.027	0.019	0.019	0.032
Pop4	Mean	35.087	3.696	2.107	0.845	0.444	0.469	0.476	0.059
ENG-SHOW	SE	0.139	0.277	0.170	0.073	0.038	0.034	0.035	0.034
Grand Mean and SE over Loci and Populations									
		N	Na	Ne	I	Ho	He	UHe	F
Total	Mean	46.207	5.261	2.859	1.153	0.559	0.597	0.604	0.067
	SE	1.424	0.190	0.112	0.039	0.018	0.017	0.017	0.014

Figure 1 shows a principle coordinate analysis plot comparing three populations of dogs: 1) Standard Poodles (both SA affected and healthy), 2) Miniature Poodles, and 3) show English Setters. The latter breed was included as a further comparison with a breed that has some structural similarities to Standard Poodles, but is known to be a distinctly different. Standard Poodles, whether healthy or SA affected, cannot be distinguished from each other, while Miniature Poodles and show English Setters are genetically distinct from Standard Poodles and each other. Only one Standard Poodle is found to cluster with Miniature Poodles and one show English Setters with Miniature Poodles.

Figure 1- Principle Coordinate Analysis (PCA) plot showing the genetic relationships of four populations of dogs -1 and 2) SA affected and healthy Standard Poodles, 3) Miniature Poodles, and 4) show English Setters.
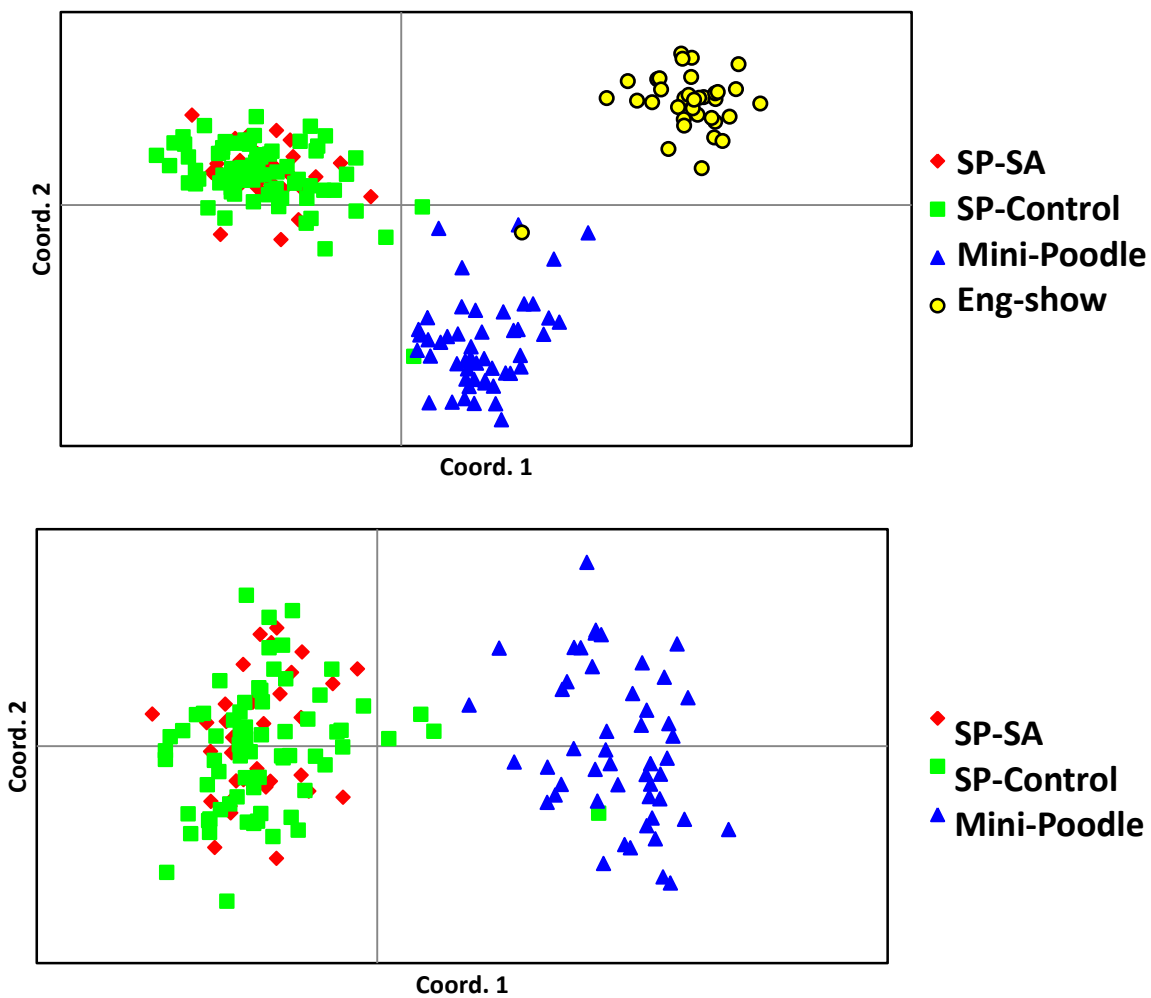

Table 2 lists the DLA class II haplotypes observed in Standard Poodles and Miniature Poodles and their frequencies within each breed. Standard and Miniature Poodles share the same major haplotype DRB1*01501/DQA1*00601/DQB1*02301 (present in 67% of Standard Poodles and 43% of Miniature Poodles). However, the two types of Poodles differ in the sharing of minor haplotypes and their prevalence. There are also a number of minor haplotypes that are unique to one type of Poodle versus the other. Therefore, DLA class II haplotyping confirms the findings

of the PCA plots. Miniature and Standard Poodles are much more genetically different than has been commonly assumed and are in fact distinct breeds that are as distant from each other as many other random breed pairings.

Table 2- DLA class II haplotype prevalence in Standard vs Miniature Poodles

haplotype ID	DRB1	DQA1	DQB1	Poodle (Standard)		Poodle (Miniature)	
number tested				315	%	34	%
1	**01501**	**00601**	**02301**	**y**	**66.7**	**y**	**42.6**
6	**01501**	**00901**	**00101**	**y**	**11.4**		
22	02001	00401	01303	y	4.6		
26	01201	00401	013017	y	1.3		
3	01502	00601	02301	y	4.4	y	1.5
4	01503	00601	02301	y	4.1	y	7.4
11	00901	00101	008011	y	2.7	y	2.9
7	**00101**	**00101**	**03601**	y	0.3	**y**	**11.8**
8	**01301**	**00101**	**00201**	y	0.2	y	5.9
5	00101	00101	00201	y	1.3	y	1.5
2	00601	005011	00701	y	0.6	y	2.9
14	00201	00901	00101	y	0.5		
16	01501	00601	04901	y	0.3		
17	01502	00601	02601	y	0.2		
31	001v	00101	00201	y	0.3		
29	10301	00101	00802	y	0.2		
30	01501	00601	02201	y	0.2		
10	010011	00201	01501	y	0.2	y	4.4
27	01101	00201	01302	y	0.5		
28	01801	00101	00802	y	0.2		
9	01501	00601	02601			y	7.4
32	00302	00101	00802			y	4.4
36	111v	00601	02002			y	2.9
13	08401	00901	00101				
15	01501	00601	00301				
18	01801	00101	00201				
20	00301	00101	00802				
21	01702	00201	01303				
33	01501	00101	03601				
12	01501	00601	02002			y	2.9
35	00802	00301	00401			y	1.5
					100		100

These findings have both positive and negative meanings. Miniature Poodles are genetically distinct from Standard Poodles and their use as controls for SA affected Standard Poodles in genome wide association studies (GWAS) is not possible, or at the least must be done with great caution. Genome wide association studies (GWAS) between SA non-affected Miniature Poodles and SA affected Standard Poodles would be complicated by genetic differences in both population structure and substructure, making it extremely difficult to determine which genetic associations were a result of SA associated genes and which associations were due to phenotypic differences. On a positive note, Miniature Poodles are both more genetically diverse than Standard Poodles and are genetically different in terms of both autosomal STR loci and DLA class II haplotypes. Therefore, larger Miniature Poodles could potentially be used to increase genetic diversity within Standard Poodles. However, such outcrossing may not eliminate either SA or Addison's disease, as judged by the occurrence of both diseases in Standard Poodle x Labrador crosses.