DogMap: An International Collaboration Toward a Low-Resolution Canine Genetic Marker Map

DogMap Consortium

DogMap is an international collaboration of 42 laboratories from 20 different countries working toward a low-resolution canine genetic marker map. The collaboration is placed under the auspices of the International Society for Animal Genetics (ISAG). The main activities focus on genetic mapping in a panel of reference families comprising 129 animals in five full-sib and three half-sib families (87 beagle and 42 German shepherd), physical mapping by FISH to anchor the linkage groups on chromosomes, and development of a database to collect, manage, and display the mapping data. The mapping is restricted to markers amenable to PCR. At the end of 1996 our map comprised 105 markers, of which 43 were assigned to 16 linkage groups. Two of those were assigned to chromosomes (L16 on CFA 18 and L13 on CFA 20). The DogMap database is still under construction. It has a two-tier structure with unpublished data, accessible to the DogMap participants, and published data, accessible to the general public. Presently the database can only be accessed using a character or graphical user interface. A major effort will be made to make the DogMap database accessible on the World Wide Web sometime in 1998. The members of the DogMap consortium are listed under "labs" at our DogMap site (http://www.cx.unibe.ch/itz/dogmap.html).

Toward the end of the 1980s genetic mapping in domestic animals made a big step forward thanks to the development of markers amenable to the PCR technique. Progress was especially remarkable in cattle and pig, economically the two most important livestock species. But the economic aspect was not the only factor responsible for this progress; equally important was the efficient collaboration between the interested laboratories. In this latter aspect the European Community (EC) played a key role by supporting PiGMaP (http://www.ri.bbsrc.ac.uk/pigmap/) and BovMap (http://locus.jouy.inra.fr/cgi-bin/bovmap/intro2.pl), genome mapping programs in swine and cattle, respectively. The major incentive for collaboration was not only common funding but the enhanced chances to secure local support based on the EC endorsement. From the beginning the participants of these two projects sought active collaboration outside the EC which led to truly global mapping programs in these two species. In other domestic species the development of genetic marker maps could not keep pace with these two collaborative efforts for reasons connected with economic importance and also specific for the species concerned.

Several factors can be made responsible for keeping the development of a canine genetic marker map on the ground up to the early 1990s. Among them the paucity of laboratories interested in this topic and the lack of loci amenable to mapping were the most prominent factors. Another major factor hampering the development of a canine genetic marker map was the lack of a standard karyotype due to the difficulty of chromosome analysis in dog. Therefore first mapping efforts were restricted to the establishment of synteny groups by means of somatic cell hybrid panel analysis (e.g., Bruns et al. 1978; Meera Khan et al. 1984; Oldenburg et al. 1987; Wilson and Adari 1987) and linkage analysis of expressed genes (e.g., Brinkhouse et al. 1973; Grosse-Wilde et al. 1983; Meera Khan et al. 1978). Only with the development of PCRable canine genetic markers, notably microsatellites (Francisco et al. 1996; Holmes et al. 1993, 1994, 1995; Mariat et al. 1996; Mellersh et al. 1994; Mellersh and Sampson 1993; Molyneux and Batt 1994; Ostrander et al. 1992, 1993, 1995; Primmer et al. 1994; Rothuizen and van Raak 1994; Shibuya et al. 1993, 1994; Thomas et al. 1997), in the early 1990s became the establishment of canine genetic marker maps feasible (Lingaas et

Authors in the DogMap Consortium are Gaudenz Dolf, Roger Batt, Etienne Bäumle, Matthew Binns, Bertram Brenig, Bob Bull, Susana Dunner, Merete Fredholm, Claude Gaillard, John Gerlach, Urs Giger, G. Goldspink, Alexander S. Graphodatsky, Nigel Holmes, Stephen Judd, Kumar Juneja, Eamonn P. Kelly, Mary G. Kent, W. Allan King, Frode Lingaas, Susan E. Long, George Lubas, Denis Mariat, Ueli Märki, Margaret Matthews, Cathryn Mellersh, Vidyanand Mohan-Ram, Karen Molyneux, Bob Morris, Tirri Niini, Jean-Jacques Panthier, Olivier Pascal, Donald Patterson, Saija Pihkanen, Ettore Randi, Nicola Reimann, Jan Rothuizen, Jeff Sampson, Armand Sanchez, David R. Sargan, Claude Schelling, Lawrence B. Schook, Gerald Stranzinger, Marek Switonski, Deryl Troyer, Alex Van De Weghe, Oscar G. Ward, Alan Wilton, Anne Katrine Winterø, and Peizhi Zhang. Address correspondence for the DogMap Consortium to Gaudenz Dolf at the Institute of Animal Breeding, University of Berne, Bremgartenstrasse 109a, Berne 3012, Switzerland. This paper was delivered at the International Workshop on Canine Genetics at the College of Veterinary Medicine, Cornell University, Ithaca, New York, July 12–13, 1997.

 90:3–6

Table 1. Comparison of the percentage of maximum LOD scores greater than a given constant simulated with 10,000 iterations using the option ISIM of the SLINK package

Type	Families	Grandparents	Parents	Offspring/ family	Total offspring	Total individuals	LOD score > 1	LOD score > 2	LOD score > 3
Full sib	24	0	48	4	96	144	68.2	36.5	16.1
Full sib	24	96	48	4	96	240	98.3	89.9	72.9
Half sib	12	0	36	8	96	132	78.1	50.2	27.6
Half sib	12	72	36	8	96	204	98.3	89.3	73.2
Full sib	12	0	24	8	96	120	85.6	62.9	39.4
Full sib	12	48	24	8	96	168	96.8	87.6	71.9
Half sib	6	0	24	16	96	120	68.7	39.7	18.7
Half sib	6	48	24	16	96	168	93.0	76.5	53.9

At locus 1 the allele frequencies were set to 0.1, 0.3, and 0.6 (PIC = 0.466), at locus 2 they were set to 0.1, 0.2, 0.2, and 0.5 (PIC = 0.610) and the true theta was set to 0.1.

al. 1997; Yuzbasiyan-Gurkan et al. 1997). Also the introduction of fluorescent in situ hybridization, techniques together with the development of a canine standard karyotype (Switonski et al. 1996), gave a boost to the physical mapping effort (Dolf et al. 1997; Fischer et al. 1996; Guevara-Fujita et al. 1996; Thomas et al. 1997).

The DogMap Consortium

In 1992 the Institute of Animal Breeding at the University of Berne (Berne, Switzerland) and the Division of Animal Genetics of The Royal Veterinary and Agricultural University (Copenhagen, Denmark) initiated the DogMap collaboration. The number of participating laboratories grew continuously during the following years. Today DogMap comprises 42 laboratories from 20 different countries. The collaboration has no common funding but shares the wish to have a canine marker map as a tool for genetic investigations in dog. Although very loosely organized, the collaboration has a structure in the form of a managing committee and scientific coordinators in the areas of microsatellite production, other markers, informatics, reference families, physical mapping, and hereditary diseases. The main purpose of these bodies is to facilitate the flow of information between the members of DogMap and to facilitate collaboration.

Goal of the Collaboration

The common goal of the DogMap participants is to contribute to the establishment of a low-resolution canine marker map with 20 cM intervals and physically anchored linkage groups. For this purpose, members of the collaboration are typing a common panel of reference families and chromosomally assigning cosmid-derived probes by FISH. Although the backbone of the emerging map consists predominantly of microsatellites, expressed loci will be included as PCRable markers for genes as they become available (Bartlett et al. 1996; Boyer et al. 1995; Burnett et al. 1995; Francino et al. 1997; Gould et al. 1995; Holmes 1994; Holmes et al. 1996; Occhiodoro and Anson 1996; Ray et al. 1996a,b,c, 1997; Shibuya et al. 1995a,b, 1996; Venta et al. 1996; Wagner et al. 1996a,b; Yuzbasiyan-Gurkan et al. 1997; Zheng et al. 1994). The mapping of genes is of paramount interest to the DogMap community since most of the participants are investigating specific canine traits, which are most often hereditary diseases. A more immediate benefit from growing canine marker maps lies in paternity testing (Binns et al. 1995; Fredholm and Winterø 1995, 1996; Zajc et al. 1994; Zajc and Sampson 1996) and genetic diversity studies (Gottelli et al. 1994; Pihkanen et al. 1996; Werner et al. 1996; Zajc et al. 1997).

The Reference Families

At the beginning of the DogMap collaboration a main concern was the establishment of a panel of reference families for genetic mapping purposes. It was then decided to use a two-generation panel, which was available within a year, instead of breeding three-generation families and delaying the typing activities. The reasoning was that the alignment of different maps would be inevitable anyway as phenotypes have to be mapped in resource families, so switching to a better panel of reference families at a later stage would not pose a novel problem. The present panel in use consists of six German shepherd full-sib families of which the 35 offspring are all half-sibs between the families and nine beagle full-sib families with a total of 71 offspring, where in two instances the offspring are half-sibs between two families.

The comparison of families with the same number of offspring but with different structure clearly shows the mapping power to be greater in the cases where the phase of the offspring is known rather than in the cases where the phase is unknown (Table 1). The average maximum LOD score in each case has been calculated using the option ISIM of the SLINK package (Ott 1989; Weeks et al. 1990). This table also shows that the number of offspring per family and the family structure influence the mapping power of a pedigree. Using the same simulation program package on our actual panel of reference families shows that the mapping power is perfectly acceptable if we deal with loci with PIC values of 0.4 or greater, which are predominantly type II markers, and genetic distances less than 20 cM (Table 2). We may not be able to initially map loci with low PIC values (<0.3), but eventually, as the map becomes denser, we will be able to tie them in, provided our families are informative.

The simulation results shown in Tables 1 and 2 demonstrate that although the mapping power varies with the family structure, any family material can be used for mapping. This is a comforting thought, since resource families for mapping specific traits often have structures far from ideal. A problem that should be seriously considered when establishing such families is the level of inbreeding. Alleles identical by descent add to the mapping power, but an increasing number of inbreeding or mating loops may prohibit making full use of this information. In the case of complex traits, it may be necessary to resort to nonparametric methods of linkage analysis if the mode of inheritance cannot be clearly established.

The DogMap Genetic and Physical Map

Several members of the DogMap community have engaged in typing the panel of reference families and in FISH mapping. A first genetic map produced within this collaboration comprises 43 loci in 16 linkage groups, of which two could be assigned to

Table 2. Comparison of the percentage of maximum LOD scores greater than a given constant simulated with 10,000 iterations using the option ISIM of the SLINK package on our actual panel of reference families

True theta	Allele frequencies	PIC	LOD score > 1	LOD score > 2	LOD score > 3
0.1	0.5, 0.5	0.375	91.3	78.3	61.9
	0.5, 0.5	0.375			
0.2	0.5, 0.5	0.375	60.7	33.8	16.3
	0.5, 0.5	0.375			
0.1	0.1, 0.9	0.164	31.4	16.2	8.0
	0.1, 0.9	0.164			
0.2	0.1, 0.9	0.164	16.1	5.8	1.8
	0.1, 0.9	0.164			
0.1	0.3, 0.3, 0.4	0.568	100	99.9	99.6
	0.2, 0.2, 0.2, 0.2, 0.2	0.786			
0.2	0.3, 0.3, 0.4	0.568	98.2	92.1	81.1
	0.2, 0.2, 0.2, 0.2, 0.2	0.786			
0.1	0.1, 0.2, 0.7	0.410	97.3	92.3	84.3
	0.03, 0.07, 0.1, 0.2, 0.6	0.543			
0.2	0.1, 0.2, 0.7	0.410	81.8	59.7	39.1
	0.03, 0.07, 0.1, 0.2, 0.6	0.543			

specific chromosomes; that is, L13 to CFA 20 and L16 to CFA 18 (Lingaas et al. 1997). The fact that not even 50% of the typed loci fall into a linkage group reflects the power of the two-generation reference families (Table 2) as well as the low prior probability to detect linkage in dog given that the loci are evenly distributed across the genome. Today more than 100 loci are typed in our reference families. So far 21 loci have been physically mapped within the DogMap collaboration (Dolf et al. 1997; Fischer et al. 1996; Thomas et al. 1997). In 14 cases the proper identification of the chromosomes concerned still await the completion of the standardization of the canine karyotype. Within the DogMap collaboration there are also resource families being typed which will provide, as a byproduct, additional mapping data to be integrated in the growing map.

The DogMap Web Site

The DogMap Web site (http://www.cx.unibe.ch/itz/dogmap.html) describes the organization and the activities of the DogMap collaboration. It also provides information on access to the DogMap database and forthcoming meetings relevant to the participants. The DogMap members are encouraged to contribute toward its continuous development.

The DogMap Database

The DogMap database has a two-tier structure—a private and a public domain. Presently the database is only accessible on the Internet using a character or graphical user interface. It provides information on the mapped loci such as linkage and synteny, physical location, primer sequences, allele numbers, PIC values for specific populations, and references. In comparison to the public domain, the private domain contains unpublished data generated within the DogMap collaboration. Details on the structure and the underlying hardware and software are available at our Web site. Because of limited resources the development of the database is advancing rather slowly. However, a major effort is being made to offer the database on the Web in 1998. Organizational improvements in the management of the database to be implemented in 1999 will ensure its currency.

Outlook

The DogMap collaboration will continue its effort toward a 20 cM marker map. In the future DogMap will actively seek collaboration with its present competitors with the goal of producing a map as fast as possible useful for addressing the genetics of hereditary diseases.

References

Bartlett RJ, Winand NJ, Secore SL, Singer JT, Fletcher S, Wilton S, Bogan DJ, Metcalf-Bogan JR, Bartlett WT, Howell JM, Cooper BJ, and Kornegay JN, 1996. Mutation segregation and rapid carrier detection of X-linked muscular dystrophy in dogs. Am J Vet Res 57:650–654.

Binns MM, Holmes NG, Marti E, and Bowen N, 1995. Dog parentage testing using canine microsatellites. J Small Anim Pract 36:493–497.

Boyer G, Nonneman DJ, Shibuya H, Stoy SJ, O'Brien D, and Johnson GS, 1995. A PCR-RFLP marker for the erythroid aminolevulinate synthase gene (ALAS2) on canine chromosome X. Anim Genet 26:206–207.

Brinkhous KM, Davis PD, Graham JB, and Dodds WJ, 1973. Expression and linkage of genes for X-linked hemophilias A and B in the dog. Blood 41:577–585.

Bruns GAP, Pierce P, Regina VM, and Gerald PS, 1978. Expression of GAPDH and TPI in dog-rodent hybrids. Cytogenet Cell Genet 22:547–551.

Burnett RC, Francisco LV, DeRose SA, Storb R, and Ostrander EA, 1995. Identification and characterization of a highly polymorphic microsatellite marker within the canine MHC class I region. Mamm Genome 6:684–685.

Dolf G, Schläpfer J, Parfitt C, Schelling C, Zajac M, Switonski M, and Ladon D, 1997. Assignment of the canine microsatellite CanBern1 to canine chromosome 13q21. Anim Genet 28:156–157.

Fischer PE, Holmes NG, Dickens HF, Thomas R, Binns MM, and Nacheva EP, 1996. The application of FISH techniques for physical mapping in the dog (*Canis familiaris*). Mamm Genome 7:37–41.

Francino O, Amills M, and Sánchez A, 1997. Canine *Mhc* DRB1 genotyping by PCR-RFLP analysis. Anim Genet 28:41–45.

Francisco LV, Langston AA, Mellersh CS, Neal CL, and Ostrander EA, 1996. A class of highly polymorphic tetranucleotide repeats for canine genetic mapping. Mamm Genome 7:359–362.

Fredholm M and Winterø AK, 1995. Variation of short tandem repeats within and between species belonging to the *Canidae* family. Mamm Genome 6:11–18.

Fredholm M and Winterø AK, 1996. Efficient resolution of parentage in dogs by amplification of microsatellites. Anim Genet 27:19–23.

Gottelli D, Sillero-Zubiri C, Applebaum GD, Roy MS, Girman DJ, Garcia-Moreno J, Ostrander EA, and Wayne RK, 1994. Molecular genetics of the most endangered canid: the Ethiopian wolf *Canis simensis.* Mol Ecol 3:301–312.

Gould DJ, Petersen-Jones SM, Sohal A, Barnett KC, and Sargan DR, 1995. Investigation of the role of opsin gene polymorphism in generalized progressive retinal atrophies in dogs. Anim Genet 26:261–267.

Grosse-Wilde H, Doxiadis G, Krumbacher K, Dekkers-Bijma A, and Kolb HJ, 1983. Polymorphism of the fourth complement component in the dog and linkage to the DLA system. Immunogenetics 18:537–540.

Guevara-Fujita ML, Loechel R, Venta PJ, Yuzbasiyan-Gurkan V, and Brewer GJ, 1996. Chromosomal assignment of seven genes on canine chromosomes by fluorescence in situ hybridization. Mamm Genome 7:268–270.

Holmes NG, 1994. Microsatellite markers and the analysis of genetic disease. Br Vet J 150:411–421.

Holmes NG, Mellersh CS, Humphreys SJ, Binns MM, Holliman A, Curtis R, and Sampson J, 1993. Isolation and characterization of microsatellites from the canine genome. Anim Genet 24:289–292.

Holmes NG, Strange NJ, Binns MM, Mellersh CS, and Sampson J, 1994. Three polymorphic canine microsatellites. Anim Genet 25:200.

Holmes NG, Dickens HF, Parker HL, Binns MM, Mellersh CS, and Sampson J, 1995. Eighteen canine microsatellites. Anim Genet 26:132–133.

Holmes NG, Shaw SC, Dickens HF, Coombes LM, Ryder EJ, Littlewood JD, and Binns MM, 1996. Von Willebrand's disease in UK Dobermans: possible correlation of a polymorphic DNA marker with disease status. J Small Anim Pract 37:307–308.

Lingaas F, Sørensen A, Juneja RK, Johansson S, Fredholm M, Winterø AK, Sampson J, Mellersh C, Curzon A, Holmes NG, Binns MM, Dickens HF, Ryder EJ, Gerlach J, Bäumle E, and Dolf G, 1997. Towards construction of a canine linkage map: establishment of 16 linkage groups. Mamm Genome 8:218–221.

Mariat D, Kessler JL, Vaiman D, and Panthier JJ, 1996. Polymorphism characterization of five canine microsatellites. Anim Genet 27:434–435.

Meera Khan P, Brahe C, and Wijnen LMM, 1984. Gene map of dog: six conserved and three disrupted syntenies. Cytogenet Cell Genet 37:537–538.

Meera Khan P, Vriesendorp H, Saisson R, Volkers WS, Los WR, and Doppert BA, 1978. Linkage between PGM3 and the genes determining the major histocompatibility complex (MHC) in *Canis familiaris* (the domestic dog). Cytogenet Cell Genet 22:585–587.

Mellersh C and Sampson J, 1993. Simplifying detection of microsatellite length polymorphisms. Biotechniques 15:582–584.

Mellersh C, Holmes N, Binns M, and Sampson J, 1994. Dinucleotide repeat polymorphisms at four canine loci (LEI 003, LEI 007, LEI 008 and LEI 015). Anim Genet 25: 125.

Molyneux K and Batt RM, 1994. Five polymorphic canine microsatellites. Anim Genet 25:379.

Occhiodoro T and Anson DS, 1996. Isolation of the canine α-L-fucosidase cDNA and definition of the fucosidosis mutation in English springer spaniels. Mamm Genome 7:271–274.

Oldenburg M, Wijnen JT, Breukel C, Berkvens TM, Brahe C, and Meera Khan P, 1987. Syntenic relationships of canine ADA gene sequences in the dog-hamster somatic cell hybrids. Cytogenet Cell Genet 46:673.

Ostrander EA, Jong PM, Rine J, and Duyk G, 1992. Construction of small-insert genomic DNA libraries highly enriched for microsatellite repeat sequences. Proc Natl Acad Sci USA 89:3419–3423.

Ostrander EA, Mapa FA, Yee M, and Rine J, 1995. One hundred and one new simple sequence repeat-based markers for the canine genome. Mamm Genome 6:192–195.

Ostrander EA, Sprague GF Jr, and Rine J, 1993. Identification and characterization of dinucleotide repeat $(CA)_n$ markers for genetic mapping in dog. Genomics 16:207–213.

Ott J, 1989. Computer-simulation methods in human linkage analysis. Proc Natl Acad Sci USA 86:4175–4178.

Pihkanen S, Väinölä R, and Varvio S, 1996. Characterizing dog breed differentiation with microsatellite markers. Anim Genet 27:343–346.

Primmer CR, Robinson NA, and Mathews ME, 1994. Canine dinucleotide repeat polymorphism at the VIAS-D23 locus. Anim Genet 25:197.

Ray K, Baldwin VJ, Zeiss C, Acland GM, and Aguirre GD, 1997. Canine rod transducin alpha-1: cloning of the cDNA and evaluation of the gene as a candidate for progressive retinal atrophy. Curr Eye Res 16:71–77.

Ray K, Tejero MD, Baldwin VJ, and Aguirre GD, 1996a. An improved test for rod cone dysplasia 1 (rcd1) using allele-specific polymerase chain reaction. Curr Eye Res 15:583–587.

Ray K, Trepanier LA, Acland GM, and Aguirre GD, 1996b. PCR/RFLP marker in the canine opsin gene. Anim Genet 27:293–294.

Ray K, Zeiss C, Acland GM, Trepanier LA, and Aguirre GD, 1996c. A highly polymorphic RFLP marker in the canine transducin α-1 subunit gene (GNAT1). Anim Genet 27:372–373.

Rothuizen J and van Raak M, 1994. Rapid PCR-based characterization of sequences flanking microsatellites in large-insert libraries. Nucleic Acids Res 22:5512–5513.

Shibuya H, Collins BK, Collier LL, Huang TH-M, Nonneman DJ, and Johnson GS, 1996. A polymorphic $(GAAA)_n$ microsatellite in a canine Wilms tumor 1 (*WT1*) gene intron. Anim Genet 27:59–60.

Shibuya H, Collins BK, Huang TH-M, and Johnson GS, 1994. A polymorphic $(AGGAAT)_n$ tandem repeat in an intron of the canine von Willebrand factor gene. Anim Genet 25:122.

Shibuya H, Collins BK, Stoy SJ, Nonneman DJ, and Johnson GS, 1995a. PCR/RFLP markers in the canine gamma-D-crystallin gene. Anim Genet 26:445–446.

Shibuya H, Mrad DR, Collins BK, Stoy SJ, Nonneman DJ, and Johnson GS, 1995b. Two polymorphisms in the canine beta-A3/A1-crystallin gene, detectable by PCR-RFLP analysis. Anim Genet 26:284–285.

Shibuya H, Nonneman DJ, Huang TH-M, Ganjam VK, Mann FA, and Johnson GS, 1993. Two polymorphic microsatellites in a coding segment of the canine androgen receptor gene. Anim Genet 24:345–348.

Switonski M, Reimann N, Bosma AA, Long S, Bartnitzke S, Pienkowska A, Moreno-Milan MM, and Fischer P, 1996. Report on the progress of standardization of the G-banded canine (*Canis familiaris*) karyotype. Chromosome Res 4:306–309.

Thomas R, Holmes NG, Fischer PE, Dickens HF, Breen M, Sampson J, and Binns MM, 1997. Eight canine microsatellites. Anim Genet 28:153–154.

Venta PJ, Brouillette JA, Yuzbasiyan-Gurkan V, and Brewer GJ, 1996. Gene-specific universal mammalian sequence-tagged sites: application to the canine genome. Biochem Genet 34:321–341.

Wagner JL, Burnett RC, DeRose SA, Francisco LV, Storb R, and Ostrander EA, 1996a. Histocompatibility testing of dog families with highly polymorphic microsatellite markers. Transplantation 62:876–877.

Wagner JL, Burnett RC, Works JD, and Storb R, 1996b. Molecular analysis of DLA-DRBB1 polymorphism. Tissue Antigens 48:554–561.

Weeks DE, Ott J, and Lathrop GM, 1990. SLINK: a general simulation program for linkage analysis. Am J Hum Genet 47(suppl):A204.

Werner P, Arnold S, Schelling C, and Hübscher U, 1996. Analysis of microsatellite polymorphisms in Bernese mountain dogs and Newfoundlands. Schweiz Arch Tierheilkd 138:152–156.

Wilson D and Adari H, 1987. The genes for galaktokinase (GALK) and uridine monophosphatase-2 (UMPH2) are syntenic in the dog (*Canis familiaris*). Cytogenet Cell Genet 46:717.

Yuzbasiyan-Gurkan V, Blanton SH, Cao Y, Ferguson P, Li J, Venta PJ, and Brewer GJ, 1997. Linkage of a microsatellite marker to the canine copper toxicosis locus in Bedlington terriers. Am J Vet Res 58:23–27.

Zajc I, Mellersh C, Kelly EP, and Sampson J, 1994. A new method of paternity testing for dogs, based on microsatellite sequences. Vet Rec 135:545–547.

Zajc I, Mellersh CS, and Sampson J, 1997. Variability of canine microsatellites within and between different dog breeds. Mamm Genome 8:182–185.

Zajc I and Sampson J, 1996. DNA microsatellites in domesticated dogs: application in paternity disputes. Pflugers Arch 431:R201-R202.

Zheng K, Thorner PS, Marrano P, Baumal R, and McInnes RR, 1994. Canine X chromosome-linked hereditary nephritis: a genetic model for human X-linked hereditary nephritis resulting from a single base mutation in the gene encoding the alpha 5 chain of collagen type IV. Proc Natl Acad Sci USA 91:3989–3993.

Corresponding Editor: Kunal Ray