**Genetic testing for feline polycystic kidney disease**

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Accepted for publication 27 October 2004

**Source/description:** Feline polycystic kidney disease (PKD) is an autosomal dominant inherited disease in Persian and Persian-related cats. 1, 2 Previously, a linkage analysis was performed by genotyping 43 feline-derived microsatellites in seven extended feline pedigrees segregating for PKD. 3 The analysis revealed significant linkage and no recombinants (Z = 5.83, θ = 0) between feline PKD and the microsatellite marker FCA476, which is within 24.2 cR of the polycystic kidney disease 1 (PKD1) gene on cat chromosome E3. 4 In this study, three microsatellites were isolated from clones of the RPCI-86 feline BAC library that contained PKD1 and PKD2 genes. Linkage analyses of these microsatellites in the most informative previously reported pedigrees further implicate PKD1 in feline PKD.

PKD1- and PKD2-containing clones were identified from RPCI-86 feline BAC library using overgo probing. 5 Sequence of the PKD1 BAC clone (GenBank accession number AC145332.26) was obtained by the University of Oklahoma’s Advanced Center for Genome Technology (Norman, OK, USA). Microsatellite primers developed from the sequence are

PKD1UCD1F: 5'-TTAAGCATTTACCGGACAC-3' and PKD1UCD1R: 5'-CATCCAGTCCAGTCTTG-3'; PKD1UCD2F: 5'-GCAAGGACCTTGAGGTG-3' and PKD1UCD2R: 5'-GCGAGGAACAGGTGAGTTG-3'. Sub-clones of the PKD2 clone were screened with a (CA)17 probe. Primer sequences for the PKD2-derived microsatellite (GenBank accession number AV727857) are PKD2UCD1F: 5'-GAAATGCACAAAAACGTG-3' and PKD2UCD1R: 5'-TCGGCTCTCTGCTGCTGTA-3' PKD1UCD2 and PKD2UCD1 have (CA)16 and (CA)19 repeats, respectively, whereas PKD1UCD1 is a (TTG)10 repeat.

Two of the original seven pedigrees (190 cats, Families 2 and 5) were analysed with these microsatellites. Polymerase chain reaction amplification, genotyping and two-point linkage analysis were performed as previously described. 3

**Linkage analyses:** Although no recombinants were found between the two PKD1-associated markers and the PKD phenotype, only PKD1UCD2 was significantly linked with PKD (Z = 5.49, θ = 0) whereas PKD1UCD1 was not (Z = 1.74, θ = 0). There was no linkage between PKD2UCD1 and the PKD phenotype (Z = -2.0, θ = 0.075). No recombinants were detected between the PKD1 markers, including FCA476, and at least two PKD1 haplotypes were identified in the non-related individuals of the two analysed families (Fig. 1). At least five disease-associated haplotypes were identified in non-related individuals with PKD (L.A. Lyons unpublished data). No individuals could be confirmed as homozygous for the disease.

**Orientation:** PKD1UCD1 is approximately 12 Kb upstream of PKD1UCD2, which is approximately 73 Kb upstream from PKD1 exon 1. FCA476 was not identified within the PKD1 BAC; hence, orientation of FCA476 to the new markers could not be determined.

**Comments:** Approximately 37% of Persians worldwide have PKD, 4–10 making it the most prominent inherited feline disease. The PKD1-linked microsatellites identified in this study could

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**Figure 1** Two feline nuclear families showing PKD associated haplotypes. Standard pedigree symbols with filled symbols implying cats affected with PKD. Unknown disease phenotypes have a question mark within the symbol. Matings are represented by the ‘node’ below the individuals. Numbers directly under or to the side of the symbols are laboratory sample identification number if >1000. Numbers <1000 are identification numbers determined by the linkage analysis software. Marker genotypes are presented below the identification numbers in the following order: PKD1UCD2, PKD1UCD1, FCA476. Allele fragment sizes been converted to single digit numbers. Genotypes are not presented for individuals that have no DNA sample. Disease haplotypes are represented in a box. Inferred genotypes are in parentheses. (a) A segment of family 2, with two disease associated haplotypes. (b) A segment of family 5.
provide a linkage-based test to predict PKD status. At least five haplotypes were identified in unrelated individuals affected by PKD, suggesting that the mutation has been in existence for an extensive period in Persians and/or these microsatellites have high mutation rates. Hence, haplotype testing for disease status prediction is not recommended in the absence of familial analysis. The markers were developed using sequence from a PKD1-containing BAC clone and are 5' to the PKD1 gene. Prior to making the test available for commercial use, analyses to investigate accuracy of this test for PKD should be performed in Persians worldwide and in other affected breeds that have used Persians for outcrosses. Breeds that are not associated with Persians and report kidney disease should confirm diagnosis of PKD using ultrasonography. Additional testing would be needed to confirm PKD1 involvement in these breeds.

Acknowledgements: Support for the research was funded by NIH-NCRR R24 RR016094, the Winn Feline Foundation, the UC Davis Center for Companion Animal Health and the Waltham Foundation (LAL) and from NIH-NHGRI grant number HG002153 (BAR). We acknowledge the National Cancer Institute for allocation of computing time and staff support at the Advanced Biomedical Computing Center of the Frederick Cancer Research and Development Center.

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