

ABSTRACT #77

IDENTIFICATION OF BETA-1 ADRENERGIC RECEPTOR POLYMORPHISMS IN CATS. BA Maran, KM Meurs, S Lahmers, OL Nelson. Washington State University College of Veterinary Medicine, Pullman, WA.

Hypertrophic cardiomyopathy (HCM) is the most common cause of feline heart disease. Beta-adrenergic antagonists (beta-blockers) are one of the most frequently prescribed treatments for affected cats; however, there is significant variation in clinician preference regarding initiation of therapy and the anticipated response. In humans, two genetic polymorphisms within the Beta-1 adrenergic receptor (β 1-AR) gene have been shown to correspond to variable pharmacologic responses. Identification of specific β 1-AR polymorphisms has allowed physicians to optimize beta-blocker therapy on a genomic basis. It is possible that cats also have polymorphisms that may impact individual response to therapy.

The hypothesis of this study is that polymorphisms are present in the feline β 1-AR gene, which could result in an altered pharmacologic response to beta-blocker therapy. The objective of the study was to sequence the feline β 1-AR gene in unrelated cats of several different breeds to evaluate for the presence of polymorphisms. The feline β 1-AR gene was amplified with specifically designed and optimized primers using the feline and human β 1-AR sequence, standard PCR techniques, and PCR-based genomic sequencing. DNA samples from 7 cats of 5 breeds (Domestic Shorthair, Maine Coon, Siberian, Ragdoll, and Bengal) were evaluated.

Two polymorphisms were identified within the β 1-AR gene, each occurring in an apparently low frequency. One polymorphism was identified in four Siberians and two Maine Coons and consists of an A/C substitution; both heterozygous and homozygous animals were identified. The change did not alter the amino acid produced. A second polymorphism was identified in two Domestic Shorthair and four Ragdolls and consisted of an AA/CC substitution. Five animals were heterozygous and one animal was homozygous for this mutation. This alteration changed the amino acid produced from Proline to Glutamine at position 277 (Pro277Gln). Computer modeling (PolyPhen software) of this region predicts a damaging structural change to the β 1-AR protein.

The clinical significance of this finding is unknown; however, the identification of β 1-AR polymorphisms in the cat could suggest variability in response to beta blocker therapy in the cat as it does in humans.