To: Fellow Yorkshire Terrier Fanciers
From: The Foundation

The Foundation has been corresponding with Dr. Sharon Center, Cornell University, regarding her work on the Portosystemic shunt microvascular dysplasia genotyping project.

We were delighted to have Dr. Center join us on one of our teleconference meetings, where she updated the Foundation on the recent progress made with this project. Dr. Center also expanded upon the direction future research will take, which is now planned to fully include the Yorkshire Terrier breed.

The Foundation was provided the following from Dr. Center:

"Our genotyping project is moving forward rapidly with extensive pedigrees, (of several hundred dogs), with matched bile acid samples and DNA extractions in Tibetan Spaniels, Cairn Terriers, Maltese, and smaller number of pedigrees for Havanese, Shih Tzu, and Yorkshire Terriers.

We needed to establish the genotyping linkage relationships in the breeds we have collected samples from during this year, before expanding the breed involvement. As we receive samples, we determine the bile acids in our lab and concurrently extract the DNA; the extractions take approximately four days and then require that we prove that the DNA functions well for genotyping. We extract the DNA from white blood cells contained in a blood sample because a cheek swab does not provide the amount or quality of DNA needed for discovery genotyping.

We have demonstrated linkage between the portosystemic vascular anomaly/ microvascular dysplasia (PSVA/MVD) trait in all breeds we have studied to the same chromosomal region. Using well-developed pedigrees in Tibetan spaniels, Cairn Terriers, and Maltese, we have identified microsatellite haplotypes that have helped narrow the region of interest. We are in the process of fine gene mapping using SNPs in this region.

Now is the time to recruit Yorkshire Terrier pedigrees. Your breed has very high priority in this study. As an Internal Medicine specialist at Cornell, I was the person that developed the bile acid test and we knew immediately after routine application of the test, that there was a problem being genetically transmitted within a number of the small breed terrier type dogs, including your breed.

I have personally treated many Yorkshire Terriers with the PSVA/MVD trait and provide telephone consultation regarding these dogs for veterinarians around the country. All large clinics that provide shunt ligation surgery have been well aware of the prevalence of the disorder in Yorkshire Terriers over the last two decades.

We believe this is an ancient mutation in the dog and it is one that involves vasculogenesis or angiogenesis: the embryologic formation of blood vessels. This disorder usually involves the portal vein and microscopic vasculature of the liver.

Until now I was devoting the majority of my attention to collecting, processing, and genotyping many hundreds of samples from Tibetan spaniels, Cairn Terriers, and Maltese so we could ascertain that we have similar linkage in well developed informative pedigrees. We needed that information before submitting a proposal for AKC support. We have submitted a proposal to the AKC and stated in that proposal, that we intend to expand the data to a larger number of Yorkshire Terrier pedigrees.
The AKC proposal is written to accomplish our genotyping endeavors and we need the funding to proceed with the project.

We wish to include the Yorkshire Terriers more extensively. I have worked with a limited number of Yorkshire Terrier breeders collecting appropriate samples from dogs with informative pedigrees. We now need to expand on this Yorkshire Terrier database. To some, this is a highly personal and emotional issue. I go to great lengths to keep every bit of information confidential."

Additionally, "Dr. Center is seeking, 200 to 300 blood samples with the following considerations:

- Dogs with high bile acids (portosystemic shunts and/or microvascular dysplasia) or proven shunts that were surgically corrected.
- Family structure is essential for the genotyping mathematical analyses. Thus blood samples from family members: sire, dam, siblings and if possible, grandparents are essential.
- Copies of pedigrees are essential.
- Single blood samples from dogs with portosystemic shunts can be submitted for association analyses.
- DNA is extracted from EDTA blood samples. Several milliliters of blood are required; the larger the sample the better for the DNA extraction.
- If bile acids have not been done on dogs, Dr. Center can arrange to evaluate samples from informative kindreds related to a dog with proven portosystemic shunt or microvascular dysplasia in her laboratory. Bile acids are evaluated using blood collected into heparin vacutainers. Discussion with coordinating veterinarians or technicians that may assist with sample collection is helpful to assure collection of high quality samples."

If you wish to participate in this project, have your veterinarian contact Dr. Sharon Center to clarify the above requirements. Contact Information is:

Sharon A. Center, DVM, DiplACVIM
Professor
Department of Clinical Sciences, College of Veterinary Medicine

Cornell University, Ithaca, NY 14853
Phone: 607-253-3060 (hospital, on page), ext. 3114 - biochemistry laboratory, audex recording)

The Foundation has provided a letter of Intent to the AKC's CHF in support of Dr. Center's grant proposal. This ongoing project finds Dr. Center projecting 18 - 24 months, or more, before a DNA marker test might become a reality for our dogs.

Furthermore, Dr. Center is encouraging breeders: "to perform bile acid testing on puppies who have attained the age where they are to be placed in new homes. Knowing that a puppy has high bile acids (in the absence of clinical illness) alerts a veterinarian that this test will not be informative at a later age for estimating liver function. For example, discovering high bile acids at a later age in a dog with microvascular dysplasia may lead to unnecessary and expensive studies."

The Foundation is currently working with the Greater New York Show Chairman, in making arrangements for Dr. Sharon Center to provide a lecture during the February, 2008 National Specialty week. The date and time will be announced when those plans are finalized.

Sincerely,

Officers and Directors of the YTCA Foundation, Inc
Sharon McCadam, Secretary