



## Announcement: New Health Projects



With great excitement, the SCWTCA Health Committee announces three new related health projects with the University of Pennsylvania Veterinary School, under the development and guidance of Paula Henthorn, Ph.D. Both SCWTCA and SCWTCA Endowment have approved funding of these projects, which have already begun.

### 1. Survey

Since the introduction of the Genetic Testing for PLN-Associated Variant Genes, Wheaten owners and breeders have wanted more information on the relationship between particular DNA results and the occurrence of PLN. This project will collect information that will allow Dr. Henthorn to perform that analysis.

To begin, an in-depth survey will be sent to Wheaten owners who have submitted DNA swabs.

- The first release of surveys will be sent to owners who submitted swabs for individual dogs. A separate email will be sent to each owner.
- The second release of surveys will go to individuals who tested entire litters, asking that the surveys be forwarded to and completed by owners of dogs with complete health testing in the last year.

The information being sought is the health status of the dogs that have been tested with the PLN Variant Alleles test. Health records (or permission for Dr. Henthorn to communicate with the veterinarian) may be requested based on the survey information obtained. This information should allow Dr. Henthorn to compare marker allele frequency to disease frequency. Such information will further enhance the assessment of risk involved in a dog's being heterozygous versus homozygous positive and thus aid breeders when researching dogs and pedigrees; it will also be helpful to owners and potential owners.

In addition, survey questions concerning PLE will be included to ascertain additional dogs that would be useful for further PLE studies. Because PLE appears to be even more complex than PLN, the more dogs participating in the study (including those confirmed affected with PLE as well as healthy geriatric dogs), the more likely we are to identify useful DNA markers.

### 2. Whole Genome Sequencing (WGS)

Since the introduction of the DNA test for PLN risk, owners and breeders have continued to hope for some similar testing for PLE. As noted, it is a more complex disease. WGS is an important component of this research.

WGS identifies essentially ALL of the DNA variants in an individual (there are millions of DNA variants within an individual mammal, compared to another member of the same species). The overall goal of

WGS (combined with other information) is to identify all of the DNA variants in healthy and disease affected dogs, then to find which of those variants are associated with disease. This is done by analyzing the genome sequences by comparing to sequences of other dogs, examining genes known to be involved with the particular or similar diseases, such as inflammatory bowel diseases for PLE, and by performing GWAS (Genome Wide Association Studies with SNP chips) to point to the chromosomal regions that need to be studied. The goal of the proposed studies, combined together, is to further improve our ability to predict the occurrence of PLN. Dr. Henthorn has submitted 10 dogs for WGS sequencing to advance to our understanding of both PLE and PLN.

This sequencing information will make a significant contribution to our PLE research. Additional sequencing would build on that information, and it is particularly important to obtain sequence from PLE and normal geriatric dogs from the U.S. population. If we are very lucky, the WGS studies will immediately identify genes for further study. More likely, as implied above, we will need to do additional GWAS (genome-wide association studies) in the future.

In particular, Dr. Henthorn will compare genome sequences from affected and healthy geriatric dogs that are 2-2 ("2s" in the SCWT vernacular) to see if we can identify DNA changes that would allow us to more accurately predict the occurrence of PLN. An added benefit of the sequencing could find a dog(s) who have a variance for both PLE and PLN.

Penn Vet is collaborating with investigators at the Children's Hospital of Philadelphia (CHOP), who study a form of IBD in very young children that appears similar to PLE in some SCWTs. If they find that the dogs have a similar genetic basis to their disease as do children, it opens the possibility of exciting collaborative work that could be mutually beneficial to dogs and kids.

We also want to sequence dogs affected with PLN and compare their genome sequences to healthy geriatric dogs (which will include the PLN 2-2 healthy geriatric dogs).

### **3. Genome-Wide Association Studies (GWAS) using SNP chips**

Because both PLE and PLN appear genetically complex (caused by the combination of DNA variations in multiple different genes as well as influenced by environmental factors), comparing the sequences of a small number of dogs is not likely to provide complete answers. GWAS will be performed after the WGS work is complete.

GWAS analysis should identify the chromosomal regions (and genes within these regions) that are associated with PLE or PLN and can then be studied in additional dogs for confirmation. This same approach was used to identify the PLN variant alleles. In the current situation, knowing the sequences of normal and affected dogs will drastically reduce the work required to go from a linked marker in a particular chromosomal region to the genes and variants that are likely to actually cause the diseases.

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**Stay Tuned:** Dr. Henthorn will report her progress and initial findings at the annual meeting in October and updates will be published regularly at [www.scwtca.org](http://www.scwtca.org) in the health section.. In the meantime, there will be some delightful fundraising items to promote and support further research in PLN and PLE. If you have any questions regarding these projects, please contact [Health@scwtca.org](mailto:Health@scwtca.org)