**Investigation of Bladder Cancer in the Shetland Sheepdog**
Updated Fall, 2022

Transitional cell carcinoma (TCC) is an invasive cancer of the bladder that is found in older dogs across every breed. More than 20,000 dogs are estimated to develop TCC each year with approximately 50% of cases involving aggressive spread of the disease to other organs. There is no cure for TCC, and life expectancy is only one to two years with current treatments. The Ostrander Lab at the National Human Genome Research Institute at NIH, in collaboration with the Purdue Comparative Oncology Program at Purdue University, are working to identify genetic variants that either increase risk for developing TCC or enhance tumor growth and metastasis. Our labs recently identified a mutation in the BRAF gene present in 85% of TCC tumors, including 100% of the Shetland sheepdog tumors tested. Interestingly, this exact mutation has been found in many human cancers including melanomas, colon cancer, thyroid cancers, and leukemias. It is our goal to accelerate advancements in both canine and human health affected by cancer.

In addition to the above, we have found that the BRAF mutation can be detected in urine from affected dogs. This discovery has the potential to aid in the development of early screening tests for TCC. Because early diagnosis is predicted to improve the prognosis of all dogs diagnosed with TCC, we are working with the Purdue Comparative Oncology Program on prescreening studies that will help determine how early in disease progression a urine based test can accurately diagnose the disease.

We have now completed the RNA sequencing of multiple TCC tumors, and are in the process of categorizing additional gene variants that interrupt cancer formation and progression. Many of these are common in both dog and human cancers, and we expect these findings to advance both human and animals therapy.

We have collected nearly 500 DNA samples from Shetland sheepdogs for multiple studies in the lab. 125 of those had a confirmed diagnosis or were suspected to have TCC. Another 126 were over the age of 10 when they were collected and had no signs of cancer. There are approximate 100 additional dogs that may have passed the age of 10 since they donated a sample and we will be contacted some of those owners to find out if their dog has remained cancer free and can be included as a Healthy Control for the TCC study.

It is important for us to maintain current health status records on the senior Shelties that make up the control group of our study. **If you have donated a sample from your healthy older dog, or you have a dog that recently turned 10, we would love to hear from you!** Please update your dog's health status by sending us an email to dog_genome@mail.nih.gov stating if your dog is still healthy, or if they were diagnosed with any type of cancer. If your dog did receive a diagnosis of cancer since their sample was submitted, please fax or scan/email the veterinarian's report to us.

If you are interested in participating in the study, please contact our Samples Manager using the contact information below. Shelties with a biopsy confirmed diagnosis of bladder cancer, or healthy Shelties over the age of 10 that have never had cancer are both eligible. You will receive a kit with a one-page consent form, return address label, a pair of vials for collecting 5-10 cc of blood at your veterinarian's office, and instructions for handling the collected sample. The collection kit is provided in a small cardboard mailer tube approved for shipping biological materials by the postal service without ice. Your participation in the study and any information you provide us will remain strictly confidential.

As always, the Ostrander Laboratory is grateful for the outstanding positive response we have received from the American Shetland Sheepdog Association and all Sheltie owners. Our research continues to thrive thanks to the outstanding support and involvement from members of your community. We thank the ASSA and everyone enrolled in the study for their help in advancing canine health research.

Sincerely,

**Heidi G. Parker, Ph.D**.
Cancer Genetics and Comparative Genomics Branch
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https://research.nhgri.nih.gov/dog_genome/

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