

## **Liquid Biopsy & Cancer Genetic Testing: Real or Meh?**

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### **Introduction**

Canine cancer necessitates early and accurate diagnostic and treatment methods for timely intervention and improved treatment outcomes. Liquid biopsy, a non-invasive and promising technique, has emerged as a groundbreaking tool for cancer detection in dogs. Cancer genetic testing also appears to be a potentially promising tool to identify potentially actionable/druggable targets.

Liquid biopsy involves the analysis of biologic fluids, such as blood or urine, to detect molecular alterations associated with cancer. This technique offers a minimally invasive alternative to traditional tissue biopsies, which can be challenging in terms of accessibility, patient compliance, and cost. Circulating tumor DNA, circulating tumor cells, and extracellular vesicles are key components analyzed in liquid biopsy, providing valuable genetic and molecular information about the tumor.

To date, the various liquid biopsy providers (PetDX, NuQ, etc.) across species have found a moderately high sensitivity (in the mid-50's) and an extremely high specificity (generally > 95-98 %). This early identification is likely crucial for implementing appropriate treatment strategies, potentially improving overall prognosis and quality of life for affected dogs. Liquid biopsy may also allow for serial monitoring of the disease, aiding in the assessment of treatment response and the detection of minimal residual disease.

Numerous challenges such as standardization of protocols, variability in sample collection, and the need for extensive field validation studies must be addressed to establish the reliability of liquid biopsy in routine veterinary practice. In conclusion, liquid biopsy and cancer genetic testing holds promise as sensitive diagnostic and therapeutic tools for canine cancer.

### **Liquid Biopsy in Veterinary Medicine**

Cancer is the leading cause of death in dogs, and many cancers are diagnosed at advanced stages. Liquid biopsy enables non-invasive detection of circulating tumor DNA (ctDNA), allowing earlier detection, tumor profiling, and monitoring. Next-generation sequencing (NGS) enables interrogation of genomic alterations, methylation, and fragmentomics in a 'pan-cancer' approach.

Clinical use cases include screening of high-risk breeds, aiding diagnosis when biopsy is difficult, molecular profiling for actionable targets, and monitoring minimal residual disease. Validation studies, such as the CANDiD study, showed overall sensitivity of ~55% and specificity ~98.5%, with much higher sensitivity for aggressive cancers such as lymphoma, hemangiosarcoma, and osteosarcoma. Other real-world studies have reported similar performance. In cats, proof-of-concept work demonstrated detection of genomic alterations in cancer patients but more research is needed.

The Nu.Q® test, developed by Volition Veterinary Diagnostics, is a blood-based cancer screening tool for dogs that detects circulating nucleosomes—chromatin fragments with cancer-associated modifications—released during cell death. Unlike sequencing-based liquid biopsy tests, Nu.Q uses a simple ELISA format, making it affordable (typically <\$150), accessible, and practical for routine veterinary use. Studies show specificity above 97% with moderate sensitivity (~50–75%, depending on cancer type), with higher detection rates for aggressive, high-shedding cancers such as

lymphoma and hemangiosarcoma. Its main clinical role is as an early warning or risk assessment tool, particularly for middle-aged or senior dogs and breeds predisposed to cancer. While it is not a stand-alone diagnostic and a negative result does not rule out disease, Nu.Q's affordability, scalability, and integration into annual wellness exams position it as a potentially valuable complement to more complex sequencing-based liquid biopsy platforms, advancing accessible cancer detection in everyday veterinary practice.

IDEXX's Cancer Dx™ panel is a newly launched, affordable blood test designed for the early detection of canine lymphoma. It detects a proprietary circulating biomarker specific to lymphoma using just a small volume of whole blood and serum, producing results in 2–3 days in the U.S. and Canada, with pricing starting as low as \$15. Pilot validation has demonstrated 79% sensitivity and 99% specificity versus healthy dogs and those with other diseases, and in ~ 60% positive cases, the test also provides B-cell or T-cell phenotype classification at no additional cost—information critical for prognosis and treatment planning. The test is intended for both diagnostic use (in dogs suspected of having lymphoma) and wellness screening (for senior dogs aged  $\geq 7$  years and at-risk breeds aged  $\geq 4$  years), and is readily incorporated into existing IDEXX wellness panels. The test became available in late March 2025, with IDEXX planning to expand the panel over the next three years to cover additional cancer types. Unfortunately there are no published studies to date on this test and it will be further discussed in the lecture.

### **Personalized Medicine and Cancer Genetic Testing**

Tissue-based genomic testing identifies mutations, copy number alterations, and fusions that may be druggable. Examples include KIT mutations in mast cell tumors and BRAF mutations in urothelial carcinomas. While tissue testing provides deeper histopathologic and molecular insights, it is invasive and sometimes not feasible. Liquid biopsy may complement or substitute in these cases, especially for serial monitoring.

Personalized medicine in pets currently lags behind human oncology due to fewer approved targeted therapies, limited clinical trials, and unclear regulatory pathways. Nonetheless, integration of genetic testing into oncology practice is expected to grow as veterinary oncology advances.

### **PetDx: OncoK9 and the Company Timeline**

PetDx, founded in 2019 in San Diego, developed OncoK9, the first multi-cancer early detection liquid biopsy test for dogs. It received Series A (\$10M, 2020) and Series B (\$62M, 2021) funding, and partnered with Petco, IDEXX, and Antech. The CANDiD validation study was published in 2022, and real-world data followed in 2023. In 2024, OncoK9 Screen, a lower-cost version, was validated. However, in March 2024, PetDx ceased processing samples due to funding shortfalls and asked veterinarians to dispose of unused kits. By early 2024, commercial operations closed.

### **Benefits, Challenges, and Future Directions**

Benefits: non-invasive testing, high specificity, multi-cancer detection, and potential for serial monitoring. Challenges include moderate sensitivity, need for extensive follow-up after positive results, lack of standardization, cost, and limited feline validation. PetDx's closure highlights financial and logistical challenges. Future directions include refining algorithms, developing guidelines for screening, and linking genetic findings with new targeted therapies.

### **Conclusion**

Liquid biopsy has shown strong specificity and moderate sensitivity in detecting canine cancers, with potential to revolutionize early detection and precision oncology in veterinary medicine. PetDx spearheaded this innovation but closed in early 2024 due to funding limitations. Future efforts should build on this foundation with larger studies, standardization, and integration into treatment strategies.

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