How Canine CGP informs diagnosis

By Dr. Guannan Wang, PhD

Most pet owners and veterinarians pursue genomic testing for its therapeutic potential, and for good reason. Effective treatments remain limited for many canine cancers. Gratifyingly, with Canine CGP's deep and comprehensive whole exome sequencing, we've had the opportunity not only to uncover the genomic landscape of canine cancers in depth, but also to identify treatment options for every case we've analyzed.

What's less obvious is that approximately one-third of the cases we've tested have also benefited from **diagnostic insights** based on genomic findings.

In human oncology, genomic mutation biomarkers have long played a role in diagnosis, particularly in hematologic malignancies and select solid tumors. For instance:

- **ASXL1** mutations are diagnostic for chronic myelomonocytic leukemia (CMML).
- **SUZ12** mutations define early T-cell precursor acute lymphoblastic leukemia (ETP-ALL).
- **IDH2** mutations are associated with a subtype of acute myeloid leukemia (AML).

These mutations often point to specific molecular subtypes, each with distinct therapeutic and prognostic implications. While veterinary medicine is still in the early stages of building this diagnostic framework, we are beginning to see promising patterns of mutation enrichment that offer important diagnostic clues, especially when traditional methods are inconclusive.

Below are a few real-world examples from our Canine CGP cases:

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1. Daisy
Daisy has a history of soft tissue sarcoma (STS) with regrowth in the left lateral thorax. Then, a splenic mass was noted. Histopathology favored hemangiosarcoma (HSA) but could not rule out metastatic STS.

Genomic insight: Canine CGP identified a PIK3CA H1047R mutation, which is frequently found in hemangiosarcoma and mammary tumors, but not typically in STS. While not exclusively diagnostic for HSA, in the context of the patient's history and tumor location, this finding supports a diagnosis of hemangiosarcoma.

2. Avery
Avery has a history of low-grade mammary carcinoma and a possible soft tissue sarcoma (STS) on the leg. She later developed hemoptysis and was found to have a lung mass, which was

cytologically consistent with carcinoma but of uncertain origin. The top differentials included metastatic mammary carcinoma versus primary lung carcinoma.

Genomic insight: Canine CGP identified an ERBB2 p.V662E (aka V659E) mutation, which is recurrent in primary canine pulmonary adenocarcinoma, but rarely found in mammary carcinoma. This finding supports a diagnosis of primary lung carcinoma, guiding cancer management decisions accordingly.

3. Kira
Kira presented with an aggressive oral tumor. Osteosarcoma was favored by histopath, but melanoma could not be definitively excluded even after IHC and second opinion review.

Genomic insight: Canine CGP revealed extensive copy number alterations and mutations in double-strand DNA repair genes (ATM, CHEK1, MRE11), along with TP53 mutation, which is a genomic profile typical of osteosarcoma, not melanoma. This finding adds strong molecular support for the diagnosis of osteosarcoma in an otherwise equivocal case.

4. Simon
Simon initially had multiple cutaneous masses diagnosed as histiocytomas that were harmless, but the masses became more widespread and irritating. Could these still represent benign, harmless tumor?

Genomic insight: Canine CGP identified two TP53 mutations, including a known hotspot (R325H) associated with malignancy and aggressive behavior due to its impact on TP53's tumor suppressor function. The presence of these mutations suggests the masses may be malignant, prompting a decision toward systemic treatment.

These are just a few examples of how Canine CGP provides valuable diagnostic support.

In summary, our test is increasingly helpful in:

- Phenotyping and molecular subtyping of lymphomas and leukemias
- Distinguishing among round cell tumors
- Distinguishing between benign versus malignant lesions
- Refining diagnoses where morphology, IHC and flow are ambiguous

Looking forward, we envision a future where **molecular diagnosis and subtyping** aids in conventional diagnosis methods, and become a standard component of cancer management in veterinary medicine, informing not just genomics-guided therapies, but also providing diagnostic and prognostication support for each patient.