

## SearchLight DNA™ Guides Cancer Diagnosis and Treatment Decisions

### OVERVIEW

- ∴ Jett, a handsome Golden Retriever, had an incidentally found intra-oral mass that was histologically identified as a poorly differentiated sarcoma, although malignant melanoma was also suspected.
- ∴ A SearchLight DNA test revealed multiple alterations, with the amplification of CDK4 and MDM2 supporting the diagnosis of melanoma. The CDK4 amplification suggested sensitivity to palbociclib, and an ATM deletion suggested sensitivity to olaparib.
- ∴ In Jett's case, SearchLight DNA supported the diagnosis of melanoma and additionally provided therapeutic options based on published biomarker associations.



Jett is a 12-year-old male neutered Golden Retriever who was noted to have a large ulcerated mass along the left buccal mucosa during an annual exam. The mass was surgically removed and was histologically identified as a poorly differentiated sarcoma, although malignant melanoma was also suspected. It was also noted to have high mitotic activity (14/10 HPF).

Staging for distant metastasis was performed after the surgery. An abdominal ultrasound revealed a large (8x6 cm) liver mass in the upper right quadrant that was cytologically consistent with a well-differentiated hepatocellular carcinoma, and thoracic radiographs did not reveal pulmonary metastasis. With no definitive diagnosis for and no evidence of distant metastatic disease from the primary oral tumor, many treatment options—including a therapeutic melanoma vaccine, chemotherapy, and radiation therapy—were discussed, along with the option to actively surveil the hepatocellular carcinoma. Ultimately, injectable chemotherapy and radiation therapy were not pursued due to Jett's age, and the melanoma vaccine was started, with consideration to alternative oral therapies.

Malignant melanoma and sarcoma are common cancers found in the oral cavity of dogs. While they are generally initially treated with surgical removal, the recommendation of additional therapy largely depends on the specific type of tumor, owing to their differences in biologic behavior. Oral melanomas have a high propensity to metastasize, with metastatic disease being a common cause of death along with local recurrence. Therefore, systemic therapy (such as chemotherapy or immunotherapy) is often discussed and recommended, with or without the addition of radiation therapy to control any residual local disease. Conversely, oral sarcomas have lower metastatic rates and pose more of a local problem, with oral tumor recurrence being most

concerning. Hence, adjuvant focal radiation therapy is often discussed for oral sarcomas, with less emphasis on systemic therapy in most cases. With these differences in biologic behavior and treatment considerations, elucidation of tumor type is essential for informing expectations and therapy.

While histopathology is the first step in distinguishing between these two cancer types, it may not be able to differentiate between the two if the tumor is poorly differentiated, as it was with Jett's tumor. Even the addition of immunohistochemistry may not be helpful, especially for the spindle variant of Jett's tumor. Therefore, SearchLight DNA was pursued for genomic support of one diagnosis over another. Jett's tumor had high-level (gain of over 40 copies) and focal (small region) amplification of CDK4 and MDM2. The co-occurrence of CDK4 and MDM2 copy number gain are common in human and canine melanoma but have not been reported in canine oral sarcomas. In addition, CDKN2B deletion (copy number loss) found in Jett's tumor also commonly occurs in canine and human melanoma in addition to many other types of cancer. These mutations and biomarker associations support the diagnosis of melanoma over sarcoma in Jett's case.

Additionally, an ATM alteration revealed potential sensitivity to olaparib (a PARP inhibitor), and the CDK4 amplification showed potential sensitivity to CDK inhibitors, such as palbociclib, abemaciclib, and ribociclib. Based on the genomic therapeutic biomarker indication, Jett was commenced on olaparib alongside the melanoma vaccine. He did not endure any side effects from olaparib, although his oral mass was noted to have regrown at his 1-month recheck exam. Radiation therapy and palbociclib were therefore discussed as alternative therapeutic options.

If you have a case you would like to share or discuss with our scientists, schedule a consultation.

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