Genomic analysis across 50 canine cancer types reveals novel mutations and putative high clinical actionability

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Oncology

INTRODUCTION

- Genomics-guided precision medicine has revolutionized human oncology.
- Simultaneously, in canine cancer, the knowledge of genomics, cutting-edge diagnostics, and therapeutics is constantly growing. (Fig.1)
- Further effort is needed, however, to comprehend the mutation landscape in canine cancers and to effectively leverage the resulting mutation-based biomarkers in clinical management.
- Here, we have utilized SearchLight DNA®, a canine cancer gene sequencing panel, to identify the mutation profiles in 813 canine cases across 53 cancer types, and assess the clinical relevance of mutation-based biomarkers in the treatment of canine cancer patients. (Fig. 2)

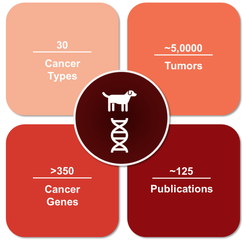

Fig. 1 – Current mutation landscape in canine cancers

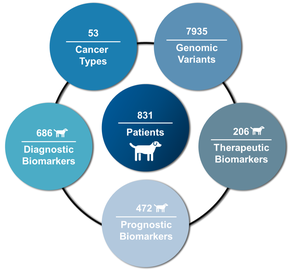

Fig. 2 – Vidium canine cancer cohort overview

METHODS

- We apply a novel workflow using SearchLight DNA, a rigorously validated next-generation sequencing-based 120-gene panel, designed to detect key cancer-driving mutation types, such as single nucleotide and indel variants (SNVs and Indels), copy number variants (CNVs), and internal tandem duplications (ITDs).
- Next, we annotate candidate pathogenic and clinically significant mutations using Vidium Insight™, a canine precision oncology biomarker knowledgebase, comprising over 4,000 mutational biomarkers associated with diagnostic, prognostic, and therapeutic implications.

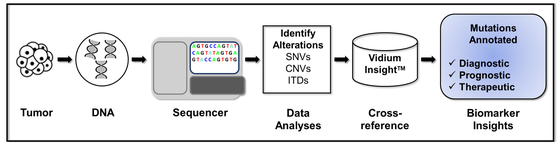

Figure 3 – SearchLight DNA workflow

RESULTS

- We identified approximately 8,000 mutations (1,061 unique) in 104 genes across 813 cases.
- Annotation of these mutations reveals the implication of key cancer genes and known oncogenic mutations based on both canine and human literature.
- Certain genes and mutations show high pan-cancer prevalence, while others display an enrichment in certain cancers. The latter can be utilized for the application of genomic-based diagnosis in cancer.

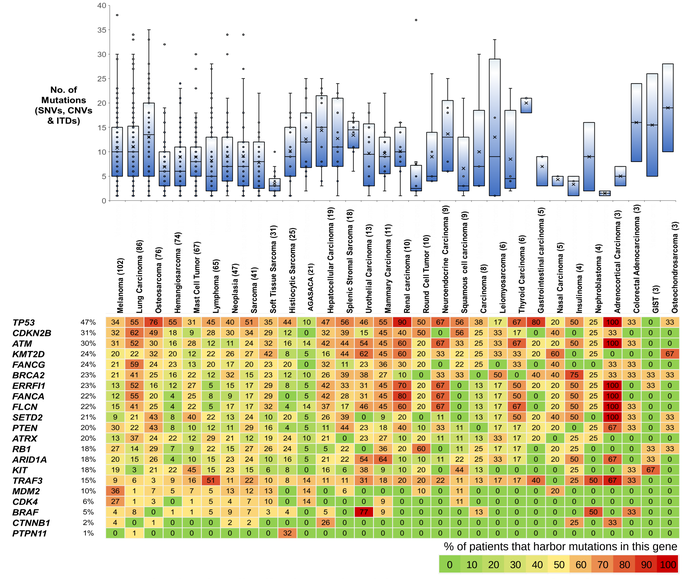

Figure 4 – Tumor mutation burden distribution and enrichment of cancer genes in select cancers

- The SearchLight-identified mutations, including SNVs, copy number gains and losses (CNG/CNL), as well as loss-of-function (LOF) mutations, exhibit potential correlations with known biomarkers, encompassing diagnostic, prognostic, and therapeutic indications.

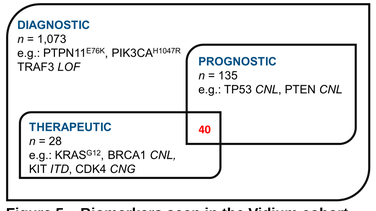

Figure 5 – Biomarkers seen in the Vidium cohort

RESULTS Cont.

- Most cancer types, both common and rare, harbor an abundance of putative mutation-based diagnostic, prognostic, and therapeutic biomarkers, based on canine data or inferred human data.

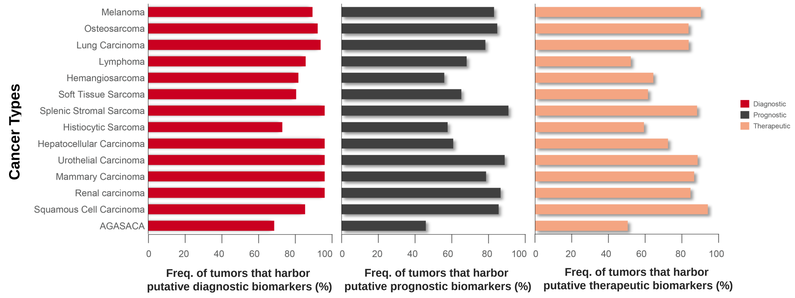

Figure 6 – Mutation-based diagnostic, prognostic, and therapeutic biomarker frequencies for select cancers

DISCUSSION & CONCLUSIONS

- In veterinary oncology, the assessment and application of mutation-based biomarkers for the clinical management of canine cancers remain challenging.
- Via the application of a novel comprehensive canine cancer gene panel, we have:
  - Validated mutation profiles for well-studied canine cancers such as mammary carcinoma, melanoma, lymphoma, and hemangiosarcoma among others.
  - Established the first-of-its-kind comprehensive genomic mutation profiles for previously under-studied cancers like renal carcinoma, hepatocellular carcinoma, and squamous cell carcinoma
  - Identified candidate pathogenic mutations, that enhance our understanding of the genomic underpinnings, and enable stratification and novel treatment development.
  - Discerned putative associations between mutation-based biomarkers and diagnoses, prognosis, and therapeutics, drawing from both human oncology insights and primary canine data.
- Our findings, we hope, will enrich enrich the clinician's arsenal in effectively managing canine cancers, and fuel future research that will ultimately lead to improved outcomes and better lives for canine cancer patients.

CONFLICT OF INTEREST DISCLOSURE

- All authors are full-time employees of Vidium Animal Health.
- SearchLight DNA® is a product developed and provided by Vidium Animal Health.