6 INTERROGATION OF SPATIAL TRANSCRIPTOMICS ON CANINE TUMOR AND NORMAL TISSUE

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Background Pre-clinical testing of combination therapies including chemotherapy, radiation, targeted and immunotherapy to treat hematological and solid malignancies can be greatly facilitated using immune competent animals with spontaneous tumors. Pet dogs are immunologically outbred, immune competent and develop spontaneous tumors such as hemangiosarcoma, astrocytoma, osteosarcoma, urothelial carcinoma, lymphoma and melanoma that share remarkable clinical, biological and genetic features with their human counterparts. Pre-clinical comparative studies for treatment of spontaneous canine tumors have incredible potential for improving understanding of human tumors and response to treatment. For this comparative approach to provide maximum information to accelerate human clinical translation of novel combination therapies and identify correlative biomarkers of therapeutic response, it is necessary to develop research tools for deep interrogation of the canine tumor microenvironment (TME). We used GeoMx® digital spatial profiler (DSP) with the novel Canine Cancer Atlas (CCA) panel to characterize spatial-transcriptomics of canine tumor and normal tissue.

Methods Tumor and normal FFPE whole resections and tissue microarray tissue across osteosarcoma, hemangiosarcoma, astrocytoma, normal colon, normal brain and lymph node from canines were profiled using DSP and by bulk gene expression using the nCounter® Canine IO panel. For DSP, each tissue was stained with organ specific immunofluorescent morphology marker antibodies, including Pan-cytokeratin (epithelial), CD45 (immune cells), Vimentin (stroma), IBA1 (microglia) or CD3 (T cells). Regions of interest were selected in various spatial areas containing tumor, stroma or normal tissue. Each tissue was profiled on the DSP using the CCA panel that contains 1962-canine specific genes using standard DSP methods.

Results We were able to spatially detect over 1800 genes across multiple tissue types from canines, including osteosarcoma, astrocytoma, melanoma, normal colon, normal brain and lymph node. Tissue specific genes were detected in spatial compartments including malignant tumor, tumor stroma and normal tissue demonstrating specific and sensitive detection of spatial-transcriptomics across a wide variety of tissue types.

Conclusions The GeoMx CCA allows for interrogation of the TME of multiple tumor types and has the potential to inform spatial biomarkers for response to therapy as well as understand mechanisms of action, as well as translate the effectiveness of these therapies to humans.

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