The tumor microbiome associates with features of the tumor microenvironment, treatment outcomes, and histologies; a national collaboration of the exORIEN Consortium


Background

A tumor microbiome has recently been established as present in many cancer types. Further study is needed to define the scope of its role in cancer tumorigenesis, progression, and treatment outcomes.

The Oncology Research Information Exchange Network (ORIEN) established a collaboration among eight member institutions to study the tumor microbiome and clinical features across several cancers.

Methods

We evaluated RNAseq data from n=2,892 tumors using the tool (exotic). Matched cancers from the Cancer Genome Atlas were processed by the same method (n=2,720 samples).

Clinical data, including treatment information, lab values, detailed histology, and long-term follow-up, were collected and harmonized across sites.

Results

For more information, contact daniel.spakowicz@osumc.edu. Research reported in this publication was supported by The Ohio State University Comprehensive Cancer Center and the National Institutes of Health under grant number P50CA016058, and the OSU Center for Clinical and Translational Science grant support National Center for Advancing Translational Sciences, Grant ID: 1UL1TR000090-05. Data access was approved by the IRB in an Honest Broker protocol (2015H0185) and Total Cancer Care protocol (2013H0199) in coordination with M2GEN and participating ORIEN members. The authors acknowledge the support and resources of the Ohio Supercomputer Center (PAS1695).

• A tumor microbiome has recently been established as present in many cancer types. Further study is needed to define the scope of its role in cancer tumorigenesis, progression, and treatment outcomes.

• The Oncology Research Information Exchange Network (ORIEN) established a collaboration among eight member institutions to study the tumor microbiome and clinical features across several cancers.

• We evaluated RNAseq data from n=2,892 tumors using the tool (exotic).

• Matched cancers from the Cancer Genome Atlas were processed by the same method (n=2,720 samples).

• Clinical data, including treatment information, lab values, detailed histology, and long-term follow-up, were collected and harmonized across sites.

Table 1. Patient Demographics. Reads that did not align to the human reference genome were filtered of (1) common laboratory contaminants, (2) taxa that inversely correlate with input RNA quantity, and (3) taxa commonly found in the negative control of microbiome experiments.

Figure 2. The eight manuscripts planned for co-submission as the exORIEN Consortium set. Additional details from one manuscript, led by Nic Denko at OSU, are shown as an example.

• Hypoxia is associated with shorter overall survival in colorectal cancer patients treated with radiation. B) Several microbes, including Fusobacterium, show a significant interaction with hypoxia for overall survival. C) Follow-up mouse experiments tested the effects of hypoxia and the immune system in a murine model of colorectal cancer. D) Both BALB/c and nude mice (lacking T-cells) show differences in tumor hypoxia following atovaquone treatment. E) The differences in the tumor microbiomes are more strongly affected by the immune system than hypoxia. F) However, some microbes are present in both high and low hypoxia tumors and alter their expression in each condition, shown here for Cutibacterium.

• Microbes were found in all tumors and associated with treatment outcomes for all modalities tested, including radiation in colorectal cancer, chemotherapy in pancreatic cancer, and immunotherapy in melanoma.

• In the case of radiation treatment in colorectal cancer, the microbes also affected outcomes in preclinical model systems and were modified by altering hypoxia levels with the drug atovaquone.

• Virus prevalence associated with histological subtypes in lung cancer.

• Similar microbes in ORIEN and TCGA tumors associated with overall survival in subtypes of sarcoma (dedifferentiated liposarcoma, leiomyosarcoma, and others).

• Finally, microbes associated with expression-based indicators of the tumor microenvironment across cancer types.

Conclusions

• These results suggest that the tumor microbiome may have broad clinical utility as a biomarker of treatment outcomes and as a target for rational manipulation.

Acknowledgements