Impact of intratumoral microbiome on immunotherapy treatment outcomes in patients with advanced non-small cell lung cancer (Abstract 1054P)

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Background and Objectives

The intratumoral microbiome (IM) associates with immune changes in the tumor microenvironment of practiveal lung cancer models. Escherichia exerts an immunomodulatory effect, reducing tumor metastasis. In patients (pts) with non-small cell lung cancer (NSCLC), the relationship between the IM and immune checkpoint inhibitor (ICI) efficacy is unknown. We sought to detect intratumoral bacteria in pts with advanced NSCLC using WGS capture-based, next generation sequencing (NGS). Based on predictive data, we hypothesized that the presence of E. coli in tumors would be associated with improved outcomes to ICI.

Detection of intratumoral microbiome in non-small cell lung cancer

Figure 1. Intratumoral microbiome detection in patients with advanced non-small cell lung cancer. Bacteria from either primary or metastatic tumor samples underwent fixation with formalin and embedding with paraffin. DNA was extracted and sequenced using the MSK-IMPACT whole exome sequencing platform. Standard tools was employed to exclude unmapped Sample Reads from the MSK-IMPACT clinical samples into FASTA files. The unmapped reads from each sample were queried for microbial content using blastn (2.9.0+) against all homologs from the NCBI database. KronaTools was then used to annotate corresponding NCBI Taxonomy to the aligned hits using the GI identifier from blastn output. If a paired end read was detected, the read was counted once. Taxorank was used to categorize each virus taxonomic ID within a specific species and genus.

Inclusion criteria and patient characteristics

Figure 3. Consort diagram (left). Only patients who underwent IMPACT testing with version 6 were included in the final cohort. Figure 4. Density plots showing proportion of un-human (purple) and bacterial reads (yellow)

Composition of the intratumoral microbiome in NSCLC using NGS-based culture-free technique

Figure 4. No template control analysis. No template control analysis (N=2536) comparing Escherichia bacterial reads across MSK-IMPACT version 3, 5 and 6. Contamination of Escherichia within the NCBI did not occur above 10 bacterial reads in the most recent version of MSK-IMPACT (version 6). Because earlier versions of MSK-IMPACT demonstrated higher levels of potential bacterial contamination, we restricted our analysis to patients who undergo NGS sequencing with MSK-IMPACT version 6 to ensure stringency in our definition of Escherichia-positive samples.

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Antibiotics use prior to tumor sampling associated with decreased intratumoral alpha diversity

Figure 6. Antibiotics use 30 days prior to tumor sampling is associated with decreased intratumoral diversity. Exposure to antibiotics as defined by receipt of antibiotics 30 days prior to tumor sampling. Fifty-five patients (7.3%) were exposed to antibiotics within 30 days of tumor sample collection. Exposure to antibiotics was associated with decreased intratumoral alpha diversity measured by Shannon index (p=0.038). Inverse Simpson (p=0.023), Gini Simpson (p=0.041) but not the Observed metric.

Intratumoral Escherichia is associated with favorable outcome to ICI

Figure 7. Association with Escherichia with outcomes to ICI. In patients treated with single agent ICI, the presence of E. coli was positively associated with PFS (median PFS 3.2 vs 2.3 months, HR 0.78, 95% CI 0.62-0.98, p=0.036). The presence of Escherichia was also associated with improved OS in this cohort (median OS 16 vs 11 months, HR 0.74, 95% CI 0.58-0.95, p=0.017). Aside from slightly older age in the Escherichia-negative group (median age 69 vs 88 years, p=0.035), there were no significant differences in baseline clinical characteristics between the Escherichia-positive and negative groups. Similar observations were not observed in the Chemotherapy group. Threshold of readcount10 was used for Escherichia positivity.

Conclusion

We characterized the intratumoral microbiome in 984 patients with advanced NSCLC. Antibiotic use within 30 days of tumor sampling was associated with decreased intratumoral alpha diversity. The presence of Escherichia was significantly associated with progression-free survival and overall survival with univariate and multivariate analyses, specifically in patients treated with single-agent ICI. The association with intratumoral bacterial load, specifically Escherichia, should be further assessed in prospective studies.

References

La Noeli, Cell Reports 2018 Goubet, Cancer Discovery 2022