CASE STUDY

Understanding immune evasion in metastatic non-small cell lung cancer (mNSCLC) with the nCounter® PanCancer IO 360™ Gene Expression panel

Who

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Product Focus

nCounter® PanCancer IO 360™ Gene Expression Panel
IO 360 Data Analysis Report, generated by Data Analysis Services (DAS)
GeoMx® Digital Spatial Profiler

Background and Objective

The introduction of immune checkpoint inhibitors (ICI) has been a paradigm shift in the treatment of NSCLC. Nivolumab is an ICI that blocks PD-1 from binding to PD-1 and is given in metastatic NSCLC (mNSCLC), among other indications. However, only 10% of patients have a meaningful response, making the detection of robust biomarkers a priority in patients' selection.

The Tumor Inflammation Signature (TIS) is an 18 gene signature in the nCounter PanCancer IO 360 Gene Expression Panel and a robust biomarker: it measures the presence of a preexisting suppressed immune response within the tumor and is associated with a positive response to ICI.

In this retrospective study, we evaluated the performance of TIS and 48 PanCancer IO 360 gene expression signatures assessing pathways associated with immune evasion in mNSCLC patients treated with Nivolumab as second-line therapy.

Study Summary and Results

FFPE tumor samples obtained from 70 mNSCLC patients — 47 adenocarcinomas (ADC), 21 squamous cell carcinoma (SCC), 2 "other" —, treated with Nivolumab, and followed for 24 months were analyzed for gene expression signatures.

We used the nCounter PanCancer IO 360 Gene Expression Panel to measure the expression of TIS and of other signatures reflecting immune-related pathways. NanoString scientists generated IO 360™ Data Analysis Reports, which included the TIS score.

Signatures associated with adaptive immune response, antigen presentation, chemokine expression, cytotoxic activity, myeloid inflammation were enriched in ADC patients but not in SCC. In contrast, pathways associated with proliferation, glycolysis, and hypoxia were enriched in SCC patients but not ADC, demonstrating a different immunological background and, likely, the intrinsic tumor cell biological characteristics characterizing the two subtypes.

"There is a big movement underway to study the microenvironments of cancers in different organs because it is known that immunotherapy doesn't work the same across different cancer types. One of the reasons for those failures is likely due to the tissue structure and the spatial relationships between the tissue and immune cells. GeoMx will be the key to us to understand those mechanisms. It will be able to see things we only dreamed about—it will be revolutionary."

—Dr. Radosevic-Robin

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When we segregated the cohort by the response to therapy, responders displayed significantly higher expression of TIS and IFNγ signature than non-responders, as well as PDL1/2, Tregs, and myeloid signatures, regardless of the ADC or SCC subtype, whereas IGF-1R pathways were associated with poor response to Nivolumab. Responder patients with smoking history also displayed significant enrichment in TIS compared to non-smokers.

Interestingly, TIS scores were significantly associated with response in KRAS-mutated but not in KRAS-wild type tumors. Thus, TIS is worth validation in other independent cohorts as a potential predictive biomarker of response to ICI in KRAS-mutated mNSCLC subpopulation which has the most aggressive course and desperately needs new treatment approaches (immunotherapy and others).

In this study we demonstrated the advantage of using the IO 360 Gene Expression Panel along with the associated IO360 Data Analysis Report to unravel the immunological differences among mNSCLC subtypes, and the potential of the Tumor Inflammation Signature as a biomarker for predicting mNSCLC patients likely to respond to Nivolumab.

Next Steps

Our next step will be to use GeoMx to see if there is a spatial relationship between the tumor and immune cells to better understand immune evasion. One of the reasons for immune therapy failures is likely due to the tissue structure and the spatial relationships between the tissue and immune cells. GeoMx will be the key to our understanding of those mechanisms.

To learn more about GeoMx DSP at NanoString, visit nanostring.com/geomx

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