Spatial proteomics identifies a biomarker associated with sensitivity to PD- 1 axis blockade in advanced NSCLC

Background

- Most patients with advanced non-small-cell lung cancer (NSCLC) fail to derive significant benefit from programmed cell death protein-1 (PD-1) axis blockade
- New biomarkers of therapeutic response are needed

Research Question

1. Can biomarkers for response to PD-1 blockade in NSCLC be identified with spatial proteomics?
2. Can spatial proteomics be used to validate PD-1 blockade response biomarkers in a large patient cohort of NSCLC samples?

Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Lung
Assay	Human Immuno-Oncology Protein Panel
Analyte	Protein Panel
Readout	nCounter® Analysis System

Why GeoMx?

"Using two quantitative and spatially informed technologies in independent NSCLC cohorts, we show that CD44 overexpression in the tumor compartment, but not in the immune compartment, predicts clinical outcomes from PD-1 axis blockade."
-Moutafi et al.

A discovery cohort of 56 patients with NSCLC treated with PD-1 axis inhibitors was assessed using GeoMx DSP. Candidate biomarkers were orthogonally validated, using the quantitative immunofluorescence (QIF) method. In addition, an external validation study was performed with whole tissue sections derived from 128 NSCLC patients treated with single-agent PD-1 axis inhibitors. Two untreated cohorts were further analyzed to address prognostic significance (n=252 from Yale Cancer Center; n=124 from University Clinic of Navarra).

Results & Conclusions

- This study represents the largest cohort to-date of patient samples analyzed by GeoMx: 136 slides representing 308 cases, 1,142 Regions of Interest (ROIs), and 2,500 Areas of Interest (AOIs)
- CD44 expression in the tumor compartment (pan-cytokeratin (pCK)+) was identified as a novel predictor of prolonged progression-free survival (PFS) (multivariate HR=0.68, p=0.043) in the NSCLC discovery cohort YTMA471.
- The effect of tumor cell CD44 in predicting PFS after correcting for programmed death-ligand 1 (PD-L1) in immunotherapy treated and untreated non-small cell lung cancer cohorts was validated.

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For more information, please visit nanostring.com/geomx

NanoString Technologies, Inc.
530 Fairview Avenue North
Seattle, Washington 98109
T (888) 358-6266
F (206) 378-6288
nanostring.com
info@nanostring.com

Sales Contacts
United States **us.sales@nanostring.com**
EMEA: **europe.sales@nanostring.com**
Asia Pacific & Japan **apac.sales@nanostring.com**
Other Regions **info@nanostring.com**

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