Models that combine transcriptomic with spatial protein information exceed the predictive value for either single modality

Background

Immunotherapy has reshaped the field of cancer therapeutics but the population that benefits are small in many tumor types, warranting a companion diagnostic test. A number of methods have been tested for their predictive value for ICI therapy but have demonstrated limited predictive ability in patients with metastatic melanoma.

Research Question

Can spatially resolved protein information acquired using the GeoMx® DSP combined with transcriptomic information from bulk mRNA gene expression acquired using the nCounter® create a more accurate predictive model for treatment associated with clinical outcome?

"In an era where immunotherapy indications are relentlessly expanding, YMMM or similarly constructed mixed modality models could be used to develop predictors for single agents or therapeutic combinations that may have distinct, compartment-specific mechanisms of action."

-Vathiotis et. al.

Experimental Setup

Instrument	nCounter®, GeoMx® with nCounter® readout
Sample Type	FFPE tissue microarray slides, matching bulk RNA
Tissue Type	Human melanoma tumor specimens
Assay	PanCancer IO 360™, 44 antibodies for GeoMx® protein detection
Analyte	RNA, Protein

Combination of mRNA and Protein Improves Best Overall Response (BOR) Classification
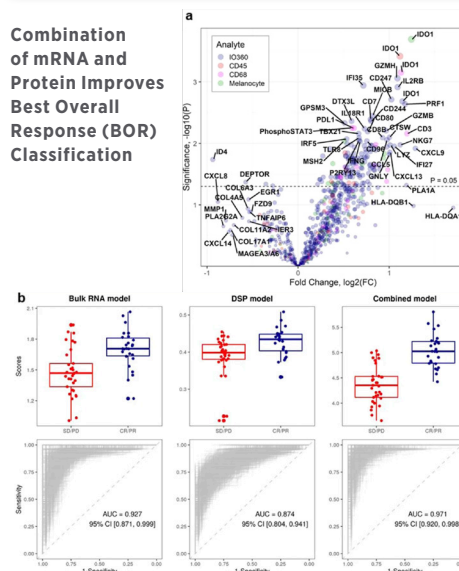

Figure 2:
a. Identification of significant predictors for predictive model generation.

b. Combined modality model is superior to RNA-only or protein-only models in terms of BOR classification.

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Results & Conclusions

- Spatial protein and bulk RNA data bear discrete, mostly nonoverlapping, pieces of biological information.

- Mixed modality (mRNA and protein) models provide more detailed and comprehensive information for immune regulation and other aspects of the tumor–stroma interaction.

- Combining mRNA and spatially defined protein information can predict clinical outcomes more accurately (AUC 0.97) than either of these factors alone.

- Work led to the creation of the Yale Mixed Modality Model (YMMM) for predicting BOR in melanoma.

Vathiotis, I.A., Yang, Z., Reeves, J. et al. Models that combine transcriptomic with spatial protein information exceed the predictive value for either single modality. npj Precis. Onc. 5, 45 (2021). **https://doi.org/10.1038/s41698-021-00184-1**

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